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Collaborative Care Toolkit Inventory: Are you ready for Collaborative Care?

Tools and approaches help all Collaborative Care teams deliver Collaborative Care. This checklist may be helpful as you assess your Collaborative Care toolkit and approach to delivering collaborative care, determine your strengths, and identify current gaps or challenges. Quality improvement approaches can help teams close gaps and incorporate necessary approaches into your Collaborative Care program.

Consider each of the following domains as your team prepares to deliver Collaborative Care.

Principle	Yes?	Tools and Approaches	
Patient-Centered Team Care	<input type="checkbox"/>	Introducing the Integrated Care Team Approach	Teams should have strategies to introduce a team care approach so patients can understand their own and other clinicians' roles.
	<input type="checkbox"/>	Team Communication Strategies	Care plans, including communication of behavioral interventions, should be shared with all team members.
	<input type="checkbox"/>	Psychoeducation	The team must provide clear and consistent psychoeducation about mental health issues and treatments. The BHP and PCP can reinforce clear information and offer written information to help patients understand information.
	<input type="checkbox"/>	Team Case Formulation	Case formulation occurs over time, but starting with a clear formulation that is patient centered and includes perspectives from the BHP, PCP, and PC can provide a more thorough initial assessment to speed effective care.
	<input type="checkbox"/>	Team Goal Setting	Patient-centered goals are important to determine as early as possible and consistently during care to inform treatment. Techniques to developing patient-centered goals should be standardized and deliberate.
Population-Based Care	<input type="checkbox"/>	Effective Engagement	Engagement and ultimately good treatment outcomes rely on a strong alliance between the patient and all providers. All team members must work together to engage the patient in treatment.
	<input type="checkbox"/>	Registry Tracking	Using a registry allows teams to track care plans and patient progress, to reach out to patients who have been identified in the registry as needing help but may have "fallen through the cracks" or who need intensification of treatment.
	<input type="checkbox"/>	Caseload Management	The whole team needs to help support an active caseload in Collaborative Care, which only includes symptomatic patients. Managing the size of the active caseload to allow access for new patients will help provide access to care to more patients.
Measurement-Based	<input type="checkbox"/>	Use of Behavioral Health Measures	All team members will need to be comfortable using common behavioral health measures. BHPs can use measures as part of



Treatment to Target			caseload management to systematically assess common mental health issues, and to promote team care.
	<input type="checkbox"/>	Measurement-Based Practice	All Collaborative Care team members will be involved in symptom assessment, progress toward clinical goals, and adjusting treatment to achieve treatment targets.
	<input type="checkbox"/>	Stepped-Care Approach	Changing care when symptoms are not improving and/or if patients are not achieving treatment goals is a key strategy of Collaborative Care. The team must be prepared to adjust psychotherapeutic approaches, medication treatments, use new modalities, or refer out to specialty care to intensify mental health care.
Evidence-Based Care	<input type="checkbox"/>	Differential Diagnosis Techniques	A good differential diagnosis and establishing a provisional diagnosis understood by the whole team is needed to inform evidence-based treatment decisions for behavioral health disorders.
	<input type="checkbox"/>	Evidence-Based Behavioral Interventions	Although ALL team members should be familiar with evidence-based behavioral interventions for health and mental health issues, the BHP will take the lead role in delivering these interventions.
	<input type="checkbox"/>	Evidence-Based Psychopharmacology	ALL team members should be familiar with evidence-based medication treatment. The PC will support the PCP to make sure the patient receives appropriate medications, and the BHP will support medication treatment compliance and track progress with dose changes.
	<input type="checkbox"/>	Suicidal and Homicidal Protocols	When patients present as imminent or high risk to hurt themselves or others, the team must have an agreed-upon protocol established within the clinic and the ability to develop a safety plan as needed.
	<input type="checkbox"/>	Crisis Management	Crises can impede treatment progress; the team must be able to address crises logistically using behavioral interventions as a team.
Accountable Care	<input type="checkbox"/>	Quality Improvement (QI) Goals	All team members should understand patient- and program-level goals. Identify key measurements and strategies to obtain data on these measures in your organization.
	<input type="checkbox"/>	QI Tools and Techniques	Continuous quality improvement of the team approach includes regular data review to identify areas for improvement. If real-time data on key measures is available, any member of the behavioral health team can examine current data on both process and outcome data to assess progress toward shared goals at both the patient and system levels. Targets for improvement can include QI related to the way treatments are delivered (both medications and psychotherapy) and team processes (such as communication about a shared care plan).





Building a Registry

Tracking patients using a registry is a critical part of Collaborative Care. Before deciding how you will use a registry, it's important to think about what clinical outcomes you want to monitor. At a minimum, processes and outcomes listed below should be tracked at both the individual patient and treating provider levels. If possible, it is also helpful to track them at the clinic (site) and organization level. These can be used as benchmarks to measure progress toward quality improvement goals and to provide technical assistance to meet those goals. Please note this is an introductory list and many other measures of short- and long-term goals could be considered.

Basic Information for Each Patient Entry:

1. Patient information
2. Contact dates (including initial assessment date)
3. Symptom severity
4. Treatment plan
5. Referrals

Clinical Outcomes:

1. Number (#) and proportion (%) of patients in treatment for at least 10 weeks achieving significant clinical improvement as measured by a validated rating scale (definition of "significant clinical improvement" varies based on the condition being measured and the measurement tool being used).
2. Proportion of patients (%) in active treatment who have a baseline measure of the clinical condition(s) being treated and the mean (average) of that score.
3. Proportion of patients (%) in active treatment who have a follow-up measure of the clinical condition(s) being treated and the mean (average) of that score.

Key Process of Care:

1. Total number (#) of patients discharged (no longer active)
2. Total number (#) of active patients
3. Proportion (%) of active patients receiving any kind of follow-up (in-person, group, phone) during past month
4. Mean (average) number of contacts since treatment started
5. Mean (average) length of time in treatment
6. Proportion (%) of patients in treatment who have been reviewed by a psychiatric consultant who has made recommendations to the primary care-based treating medical/behavioral health providers
7. Proportion (%) of patients in treatment for at least 10 weeks who are not improved and who have not been reviewed with the psychiatric specialist



Sample Registry

Patient #	Tickler	Patient Information			Contact Dates			Depression Severity	TREATMENT		REFERRAL (OPTIONAL-Process)		
Follow-up Contact number	Action	Name	ID #	Phone	Start Date	Date follow up due	Actual contact date	PHQ Score	Current Rx (Name,Dose,Freq)	Tx Plan (Cont. Med, Pleasant Activity, Comments)	Contact duration (if med)	Type of Contact (e.g. phone, in person)	Decision Initials
Patient 1													
1			0	0				#02/01					
2			0	0				#01/01					
3			0	0				#00/01					
4			0	0				#01/01					
5			0	0				#01/01					
Patient 2													
1			0	0				#01/01					
2			0	0				#01/01					
3			0	0				#01/01					
4			0	0				#01/01					
5			0	0				#01/01					

Patient #	Tickler	Patient Information			Contact Dates			Depression Severity	TREATMENT		REFERRAL (OPTIONAL-Process)		
Follow-up Contact number	Action	Name	ID #	Phone	Start Date	Contact date	PHQ Score	Change in PHQ Score (minimum larger or 40% within 10 weeks of treatment initiation or change)	Current Rx (Name,Dose,Freq)	Tx Plan (Cont. Med, Pleasant Activity, Comments)	Contact duration (if med)	Type of Contact (e.g. phone, in person)	Decision Initials
Patient 1													
		Genevieve	1022-206-351-8889	506/05			19		Varalacine 18.273 mg	Start medication, patient education	00	/	
1		Genevieve	1022-206-351-8889		5/06/05	17	-11%		Varalacine 18.71 mg	increase dose, pleasant activity scheduling	20	/	
2		Genevieve	1022-206-351-8889		5/06/05	16	-16%		Varalacine 18.74 mg	cont. med, Pleasant activity scheduling	20	/	
3		Genevieve	1022-206-351-8889		5/27/05	17	-11%		Varalacine 18.100 mg	increase dose, pleasant activity scheduling	30	/	
4		Genevieve	1022-206-351-8889		6/5/05	15	-21%		Varalacine 18.100 mg	cont. med, Pleasant activity scheduling	20	/	
5		Genevieve	1022-206-351-8889		6/18/05	13	-32%		Varalacine 18.100 mg	cont. med, Pleasant activity scheduling	20	/	
6		Genevieve	1022-206-351-8889		7/2/05	16	-16%		Varalacine 18.100 mg	cont. med, Pleasant activity scheduling	20	/	
7		Genevieve	1022-206-351-8889		7/15/05	14	-26%		Varalacine 18.226 mg	increase dose, pleasant activity scheduling	30	/	
8		Genevieve	1022-206-351-8889		8/1/05	13	-32%		Varalacine 18.226 mg	cont. med, Pleasant activity scheduling	20	/	
9		Genevieve	1022-206-351-8889		8/15/05	11	-42%		Varalacine 18.226 mg	cont. med, Pleasant activity scheduling	20	/	
10		Genevieve	1022-206-351-8889		8/25/05	12	-37%		Varalacine 18.226 mg	cont. med, Pleasant activity scheduling	10	P	
11		Genevieve	1022-206-351-8889		8/15/05	9	-53%		Varalacine 18.226 mg	cont. med, Pleasant activity scheduling	20	/	

Using an EXCEL®-BASED REGISTRY TOOL

<http://aims.uw.edu/resource-library/using-excel%C2%AE-based-registry-tool>





Template: Initial Care Manager Assessment & Care Plan: This template and example initial assessment can guide your organization's delivery and documentation of collaborative care. The prompts for each section can help the care manager know what to say help to structure the initial assessment and to be efficient in collecting complete assessment information. There is also a completed example of the initial care manager assessment and care plan of a fictional patient for reference.

Introduction to Collaborative Care

- Thank you for working with me!
- A team will be taking care of you—but you are the captain of the ship
- Care Manager Role—assessment, offer treatment options and coach/focused psychotherapy
- Help you use tools to manage your behavioral health symptoms
- Team will communicate about your care including recommendations from psychiatric consultant
- Continue to contact Primary Care Team for all illnesses and acute problems

Patient Concerns

- When did you start feeling like this?
- Have your symptoms changed during this time?
- Have they changed recently?

Assessment

Behavioral Health History

Have you ever struggled with _____?

Mood Symptoms

Depression:

Bipolar Disorder/Mania:

Anxiety Symptoms/Trauma History

Psychotic Symptoms/Hearing

Substance-Use Disorder

Other Behavioral Health Concerns

Safety Concerns

Current Safety Concerns? Flag
as Safety Risk?

Prior Behavioral Health Treatment

Inpatient Hospitalization?

Outpatient Mental Health Treatment/Psychotherapy?

Past Medications?

Past Safety Concerns?

Social History

We will be getting to know each other better over time. For now, what are the important things that I should know about you?

Education:

Employment:

Family/Culture/Childhood:

Legal History:

Social Supports:

Barriers to Self-Care/Basic Needs:

Living situation/Lives With

Employment Status:

Hobbies:





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Significant Medical Problems and History

-Tell me about your current medical problems.

Current Medications

-What are your current medications? How do you take them?

-It's hard for most of us to take medications regularly. Is that a problem for you?

Patient Goals for Treatment

Mental Status Examination

Validated Behavioral Health Measures

Summary of Problems/Provisional Diagnosis

Plan

Treatment options discussed:

Schedule Follow-up:

Care Manager:

PCP:

Discuss with Psychiatric Consultant?





Example: Initial Care Manager Assessment & Care Plan: This is a completed example of the initial care manager assessment and care plan for reference for a fictional patient.

Introduction to Collaborative Care

Reviewed with patient

Patient Concerns

Patient is a 26 yo male presenting with concerns of anxiety. He reports a long history of anxiety dating back to childhood. This has made it difficult for him to be able to work because he becomes anxious around other people. Endorses some depression symptoms but feels this is secondary to ongoing anxiety. Sleep: no concerns, 7–8 hours per night. Appetite: no concerns.

Assessment

Behavioral Health History

Mood: Depression: No previous history, some symptoms now related to limitations for anxiety per patient. Bipolar: Denies any history of mania or decreased need for sleep.

Anxiety: Significant worry since childhood. Reports onset of anxiety was in 2004 when patient's Dad moved out—this same year, patient dropped out of school (9th grade) and left the church. Pt identifies anxiety symptoms as isolating, avoiding leaving the house, anxiety around interacting with others, especially strangers, anxiety about social awkwardness and worry about the perception of others. Pt reports rarely leaving home, he avoids thinking about his situation and distracts himself with television and reading. Describes feeling frustrated because he understands what the problem is, but cannot overcome the anxiety. Denies Panic symptoms. Denies OCD symptoms. Denies domestic violence/PTSD symptoms/Trauma.

Psychotic Sxs: denies

Substance Use: denies any history of or current substance use

Other: Reports ADHD symptoms—difficulty concentrating since 2004

Safety Concerns

Suicide Attempts: denies Current Suicidal Ideation: endorses passive S/I, denies plan; denies intent

Prior Behavioral Health Treatment

Some counseling in high school. No other psychotherapy or outpatient mental health. No in-patient hospitalizations. No previous medication trials.

Social History

Birth/Childhood: grew up in a rural WA. Pt reports his Dad was an alcoholic and abused pain medication. His Dad left in 2004 when pt was 12 yrs old. Shortly after his Dad left home, pt dropped out of school and stopped attending church, which had been his primary social and support network. Family: Current Status: single Children: none Parents: divorced Siblings: one older and one younger. Education: dropped out school in 9th grade—recently completed GED. Employment: fast food for one year—interested in going to work. Legal Hx: denies

Significant Medical Problems and History

Other medical concerns: none

Head Injury/Unconscious: denies

Seizure Disorder: denies

Current Medications

None



Patient Goals for Treatment

Pt had difficulty identifying any interest areas, both past and present

Mental Status Examination

Appearance: appropriate/casual dress, hygiene good

Eye Contact: minimal

Speech: normal

Mood/Affect: anxious

Attitude: discouraged

Thought Process/Content: unremarkable

Validated Behavioral Health Measures

GAD-7: 15

PHQ-9: 13

MDQ: Negative

AUDIT: Negative

Summary of Problems/Provisional Diagnosis

Anxiety NOS (GAD vs Social phobia); Adjustment disorder with depressed features vs MDD

Plan

1. Pt has not taken medications in the past and is not interested in medications at this time.
2. Discussed CBT for anxiety and relaxation approaches to manage anxiety symptoms. Patient will be referred to DVR for help with job search.
3. Follow up with PCP in one week. Follow up with care manager in 2 weeks.
4. Will discuss possible medication options if need to intensify treatment with psychiatric consultant this week.





Template: Follow-up Care Manager Note: The following template shows a sample care manager follow-up note. The note should be organized and focused. Note can be brief—summarizing patient progress and agreed-upon next steps. There is also an example follow-up care manager note of a fictional patient for reference.

Symptom Check

Check-in: How was your week?
Ask to complete appropriate behavioral health measures.
Discuss any changes.
If started on new medication: How's it working? Able to take every day? Any side effects?
If working on psychotherapy of other behavioral targets: How is it going?

Treatment Review

Medications

Let's take some time to check our clinic information and make sure the medications are written correctly.
It's hard for most of us to take our medications every day. How are you doing with _____?
Check each medication for dosage, timing, and number of times taken last week.
Troubleshoot problems with medications not being taken as ordered.

Behavioral Treatment Review

Describe your current progress on behavioral strategies.
What success have you had? Reinforce any gains however small.
Have you had any challenges? Help adjust goals and engage appropriate treatment.

Referrals

Did you connect with the referral? Problem-solve any challenges.

Assessment/Provisional Diagnosis

Progress toward Goals

What are they currently doing well?
Do we need to intensify treatment?
Other options supported by research. What else do you think might be helpful?

Care Plan

Medication Treatments Reviewed

Behavioral Treatments Reviewed

Referrals

Schedule Follow Up

- Remind of any outstanding tests or follow-up due.
- Complete care plan and review.
- Set next appointment. Care manager? PCP?
- Do you need to discuss patient psychiatric consultant?
- Care plan updates communicated to PCP?

Time Spent: _____





Example Follow-up Care Manager Note: This is an example follow-up care manager note of a fictional patient for reference. Ideally this note would be available for the whole team to reference the integrated care plan.

Symptom Check

Patient reports ongoing symptoms of daily flashbacks, nightmares, and anxiety about being home alone—symptoms often so significant she experiences rapid breathing and stomach tightness. Patient encouraged to discuss situations that make her anxious, patient reports feeling lonely especially in evening.

Treatment Review

Patient continues to take her sertraline and only missed one dose last week. Discussed strategies to continue daily compliance. Patient referred to support group for women. Patient also assisted in rewording resume for employment search and referred to job placement organizations in her community.

Assessment/Provisional Diagnosis

Patient is a 51yo female seen for ongoing treatment of PTSD.

Care Plan

Discussed need to continue to take sertraline daily. Reviewed options to target residual symptoms with adjustment of medication and/or new medication to target nightmares and patient is interested. Discussed starting behavioral activation at next visit. Patient plans to follow up with job placement organizations before next visit.

Time Spent: 30 minutes





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Template: Relapse Prevention Plan: The following template shows a sample relapse prevention plan. Relapse prevention plans show the progress that a patient has made and provide clear direction for how to reconnect to care as needed. There is also an example relapse prevention plan of a fictional patient for reference.

Date: _____

Purpose: Behavioral health episodes can occur again during a person's lifetime. The purpose of a relapse prevention plan is to help you understand your own personal warning signs. These warning signs are specific to each person and can help you identify when symptoms may be starting to return so you can get help sooner—before the symptoms get bad. The other purpose of a relapse prevention plan is to help remind you what has worked for you to feel better. Both of these put YOU in charge!

Instructions: 1. Fill out this form with your care manager. 2. Put it where you'll come across it on a regular basis. 3. If you see signs of returning symptoms, use your prevention plan.

My Diagnosis: _____

Maintenance medications

1. _____ ; _____ tablet(s) of _____ mg _____ Take at least until _____
2. _____ ; _____ tablet(s) of _____ mg _____ Take at least until _____
3. _____ ; _____ tablet(s) of _____ mg _____ Take at least until _____
4. _____ ; _____ tablet(s) of _____ mg _____ Take at least until _____

Call your primary care provider or your care manager with any questions (see contact information below).

Other treatments

1. _____
2. _____
3. _____

Personal warning signs

1. _____
2. _____
3. _____
4. _____

Things that help me feel better

1. _____
2. _____
3. _____
4. _____

If symptoms return, contact: _____

Primary Care Provider _____ **Phone:** _____ **Email:** _____

Care Manager _____ **Phone:** _____ **Email:** _____

Next Appointment Date _____ **Time:** _____





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Example Relapse Prevention Plan: This is an example relapse prevention plan of a fictional patient for reference.

Date: May 31, 2015

Purpose: Behavioral health episodes can occur multiple times during a person's lifetime. The purpose of a relapse prevention plan is to help you understand your own personal warning signs. These warning signs are specific to each person and can help you identify when symptoms may be starting to return so you can get help sooner—before the symptoms get bad. The other purpose of a relapse prevention plan is to help remind you what has worked for you to feel better. Both of these put YOU in charge!

Instructions: 1. Fill out this form with your care manager. 2. Put it where you'll come across it on a regular basis. 3. If you see signs of returning symptoms, use your prevention plan.

My Diagnosis: Major depressive disorder

Maintenance medications

1. Sertraline ; 1 tablet(s) of 100 mg Take at least until discuss with PCP
2. ; tablet(s) of mg Take at least until
3. ; tablet(s) of mg Take at least until
4. ; tablet(s) of mg Take at least until

Call your primary care provider or your care manager with any questions (see contact information below).

Other treatments

1. Behavioral Activation for depression: Continue to look for regular time for your art
2. Sleep hygiene: Keep up the good work with a regular bedtime and wake time!
- 3.

Personal warning signs

1. I sleep more than 8 hours a night.
2. I stop painting.
3. I stop answering phone calls from my friends.
- 4.

Things that help me feel better

1. Walking my dog.
2. Painting!
3. Taking my medications.
4. Talking with my friends. Calling Sarah

If symptoms return, contact: My PCP at Anytown Health Center 555-111-2222

Primary Care Provider: Mary Smith, MD Phone: 555-111-2222 Email: Use the patient portal

Care Manager: John Black Phone: 555-111-2222 Email: Use the patient portal

Next Appointment Date Dr. Smith 7/22/15 Time: 9:00 AM





Template: Psychiatric Consultant Case Review: The case review is shared by the psychiatric consultant and the care manager and typically is structured so that 6–8 patients can be reviewed every week. This case review template can facilitate structured gathering of information. Content for this summary would include information from the case manager and psychiatric consultant discussion. There is also an example psychiatric consultant case review of a fictional patient provided for reference.

Summary:

Depressive symptoms

Bipolar disorder screen

Anxiety symptoms

Past treatment

Suicidality

Psychotic symptoms

Substance use

Other

Functional

Impairments

Psychosocial factors

Medical problems

Current medications:

Medication

Dosage

--	--

Goals: (Patient centered)

Assessment/Provisional Diagnosis:

Recommendations:

- Evidence-based brief behavioral interventions
- Evidence-based psychopharmacology
- Other important goals for the team to focus on





Example Psychiatric Consultant Case Review: This is an example of an initial psychiatric consultant case review generated of a fictional patient after weekly psychiatric consultation. This note summarizes the discussion with the care manager, taking into consideration records from the EMR. Typically this note would be made available to a PCP and placed into the EMR for reference by the whole team. Ideally, this note would be updated if the patient needed further intensification of treatment in the future.

Summary: Patient is a male presenting with 3 months of depression and anxiety in the context of motorcycle crash in 2012.

Depressive symptoms: Moderate **Bipolar Screen:** Denies **Anxiety symptoms:** Moderate; PTSD symptoms related to motorcycle accident and prison history **Past Treatment:** None **Suicidality:** Denies **Psychotic symptoms:** Denies **Substance use:** History of use; Denies current use **Other:** None **Functional Impairment:** Unemployed, limited social contacts **Psychosocial factors:** has 2 kids, owes child support, very close with his kids; history of prison now off probation **Medical Problems:** hypertension; chronic Pain for 2 years related to herniated disc

Current Measures: PHQ-9: 16 GAD-7: 12 AUDIT: Negative MDQ: Negative No

Current medications:

Medication	Dosage
Acetaminophen-OxycodoneHCl (Percocet)	1 tablet of 325-5 mg twice a day (Daily Dose: 650-10 mg)
Metoprolol Tartrate (Generic)	1 tablet of 50 mg once a day (Daily Dose: 50 mg)
Polythiazide-Prazosin HCl (Minizide)	1 tablet of 0.5-1 mg at bed (Daily Dose: 0.5-1 mg)

Goals: Wants to look forward to visits with children, wants to feel less restless at night experience less pain, pain; Benefits/DVR

Assessment/Provisional Diagnosis: MDD; PTSD

Recommendations:

- 1) Start citalopram to target depression and anxiety; Week 1: Baseline weight. Consider BMP for baseline sodium in older adults and baseline QTc in all patients. Start Celexa 10 mg qday. Week 2: Increase dose to 20 mg qday. Week 3 and beyond: Consider further titration upward to 40 mg qday as tolerated (except in older adults). **Typical target dosage:** 40 mg/day. **Max dosage:** 40 mg qday
- 2) Can consider titration of prazosin to target nightmares; Week 1: Prazosin 1 mg qhs increase to 2 mg qhs after 3–4 days. Week 2: Assess for side effects; Continue titration in 1 mg qhs increments every 3–4 days until symptom remission, limiting side effects or max dose reached. **Typical target:** 3–5 mg qhs. **Usual Max:** 10 mg qhs (in severe PTSD).
- 3) Continue close contact with care manager for psychosocial support; Consider CBT for pain





Template: Psychiatric Consultant Follow-up Note: The psychiatric consultant may provide a follow-up case review. This template is an example of how to provide a brief, focused note to provide additional recommendations, especially when intensifying treatment. There is also an example psychiatric consultant follow-up note of a fictional patient provided for reference.

Summary:

Medical problems:

**Barriers to
employment:**

Current medications:

Medication

Dosage

--	--

Behavioral health measure scores

Goals:

Assessment:

Recommendations:

- Evidence-based brief behavioral interventions
- Evidence-based psychopharmacology
- Other important goals for the team to focus on





Example Psychiatric Consultant Follow-up Note: This is an example psychiatric consultant follow-up note of a fictional patient provided for reference. The care manager would be responsible for making sure this information was communicated to the whole team.

Summary: Patient is a 40 y/o female initially presenting with depression. Some depression improvement initially with decrease in PHQ9 score from 20 to 14, but now with more depression as off the Seroquel because she cannot afford it.

Medical Problems: Knee replacement, chronic pain, high cholesterol, osteoarthritis in back, fibromyalgia, irritable bowel, hypothyroidism, TMJ, major depression, anxiety, blepharitis. **Barriers to employment:** Pain, Depression, Economy

Current Measures: PHQ9: 14

Current medications:

Medications	Dosages
†Bupropion HCl (Generic)	1 tablet of 150 mg BID
†Citalopram Hydrobromide (Generic)	1 tablet of 40 mg every morning (Daily Dose: 40 mg)
†Cyclobenzaprine HCl (Generic)	tablet of 10 mg PRN
†Levothyroxine Sodium (Generic)	1 tablet of 175 mcg once a day (Daily Dose: 175 mcg)
†Quetiapine Fumarate (Seroquel)	1 tablet of 50 mg at bed

Goals: Reduce depression; Better engagement in medical care

Assessment: MDD; Anxiety NOS; h/o ADD

Recommendations:

- 1) Continue citalopram 40 mg to target depression and anxiety, bupropion to 150 mg bid for depression and as a second line ADHD medication,
- 2) Explore options to restart the quetiapine to 50 mg target depression augmentation. Week 2: Increase in quetiapine to 100 mg QHS. Week 3: Increase in quetiapine to 150 mg QHS. Usual dosage range: 150–300 mg/day.
- 3) Continue close contact with care manager
 - a. Pleasant events scheduling; consider more formal behavioral activation
 - b. Sleep hygiene
 - c. CBT for thought distortions.





A Guide for Developing Primary Care Protocols for Psychiatric Emergencies

Patient and provider safety is important in every primary care clinic. Providers have a duty to protect patients, themselves, their colleagues, and potential victims. It is helpful to develop a team protocol for managing psychiatric emergencies such as severe suicidal ideation in the primary care clinic. This example is intended to help primary care clinics develop their own specific protocol(s) for psychiatric emergencies.

Principles:

1. **Know who to call and have the information easily available to everyone in the clinic.** All clinic employees, not just the behavioral health staff or the clinic manager, should have access to this information. Don't wait until you need the information to make sure that you have the phone number for the local crisis line or mental health crisis team easily available.
2. **Don't use safety contracts.** Safety contracts have no legal meaning and may give a false sense of security to the clinician. Safety contracts do not reduce the likelihood of suicidal or violent behavior. A contract is not an adequate substitute for a thorough assessment and appropriate intervention. Just because a patient says they will call you before they take action doesn't mean that they will.
3. **Take threats seriously.** Although suicide is a rare event, make sure to assess each patient who is having suicidal thoughts.

Suicidal Patients

Over 30,000 people die by suicide yearly, and over 650,000 attempt suicide. Men are more likely to complete suicide, whereas women are more likely to attempt suicide. Risk factors include being male, white, psychiatrically ill, having a substance abuse problem, and being socially isolated. Modifiable risk factors include anxiety and physical pain. The greatest risk factor for suicide is a past attempt, with the highest risk coming within a few months after the prior attempt.

Older, divorced or widowed, alcoholic, white males have the highest rates of suicide. The #1 method of death by suicide involves a firearm. Because of this, reducing access to guns is a major part of suicide risk reduction. Other common causes are asphyxiation and poisoning.

A completed suicide is rare (even in mental health settings) but is a major source of stress and worry for providers. It is also very difficult (at times devastating) for those left behind. This is important to discuss with patients when there is a sense they have talked themselves into the fact that everyone would be better off if they were dead; discuss with them what is concretely keeping them from attempting suicide right now.

A clinic protocol needs to include, at a minimum, the following: 1) a plan for screening those at risk for suicide, 2) education about gathering further information once a patient has screened positive for thoughts of suicide, and 3) a triage plan for determining who needs to be sent to an emergency room immediately versus being followed in outpatient care.





Step 1: Screening

Any patient presenting for evaluation of a psychiatric or substance abuse problem should be screened for thoughts of suicide. This is a standard part of the mental status exam. This can be accomplished using question #9 from the PHQ-9:

“Have you been having thoughts that you would be better off dead or thoughts of hurting yourself in some way?”

Step 2: Gathering Further Information

Any patient who reports thoughts of suicide should be interviewed in more detail regarding the nature of those thoughts, plans that are in place, a history of past self-injury, and the current social environment in which the patient is embroiled. Some questions could include the following:

1. ***Have you already done something to hurt yourself?*** The patient may describe a “dry run” or an attempt that occurred shortly before your evaluation. At this point, the patient should be referred for emergency evaluation.
2. ***Do you have a plan to commit suicide?*** It is appropriate to ask the patient what the plan might be and what effort he or she has gone through to bring about that plan in the future. This involves questions about the means (guns, pills, hanging, carbon monoxide poisoning, others), the potential for rescue if the attempt occurs, and the intent behind the possible attempt (i.e., is there an unambiguous wish to die).
3. ***Have you been struggling against thoughts about hurting yourself or committing suicide?*** Often, patients with major depression have intrusive, unpleasant thoughts about suicide that are frightening to them. This question clarifies the degree to which the patient has been preoccupied with thoughts of suicide.
4. ***Have you attempted to kill yourself in the past?*** Past attempts at self-injury place patients at higher risk for suicide. If a patient answers this question, it is appropriate to ask them what happened and what type of treatment was required. (Were they hospitalized medically or psychiatrically?)
5. ***Do you have anything in place (such as family or other social supports) to help keep this from happening?*** A patient with no social supports who has made no efforts for self-protection may be at high risk for suicide.

Step 3: Inpatient or Outpatient Treatment

The final step, once information has been gathered, is to determine if the patient can continue to be treated in the outpatient setting or be referred for hospitalization. Some factors useful in guiding this decision:





Outpatient Treatment: A patient who describes no clear plan, no clear wish to be dead, no history of self-injury, and fair social and family supports may be appropriate to manage as an outpatient. Other important clinical factors include the degree to which you know the patient, the ability for close follow-up with the patient, and other comorbid problems (like substance abuse, personality difficulties, and legal problems). One simple rule to go by: if you do not feel comfortable sending the patient home with an outpatient plan, then consult with your team on how to modify the plan.

If the decision is not to send the patient to the ER for possible inpatient admission, it is important to address modifiable risk factors as much as possible. For example, could pain or anxiety be treated right away or are there drug side effects (like akathisia) making it hard for the patient to feel comfortable? While giving hope about the treatment of depression, ask the patient what keeps him or her alive and reinforce those factors as much as possible. If there are any lethal means available, work with the patient (or family) to get rid of those. Close follow-up by you or someone else is vital if you have decided on outpatient treatment for a patient with thoughts of suicide.

Inpatient Treatment: A patient with a plan for suicide, persistent thoughts of suicide, and past suicide attempts should be sent to an emergency room for evaluation. In addition, if there is no good follow-up plan and you do not know the patient well, referral for inpatient evaluation should also be made. In fact, if you cannot be convinced that there is a good outpatient alternative for the patient, he or she needs to be evaluated at a local emergency room.

Step 4: Emergency Evaluation: What to Do Next?

If you have decided the patient needs to be in the hospital, the first thing you should do is tell the patient what you think the appropriate thing to do is for his or her safety. This can be a great relief to patients and often they will participate in whatever needs to be done next. That could include:

Direct admission to an inpatient unit: While keeping the patient safe in the clinic, contact the patient's insurance carrier and obtain authorization for a psychiatric admission. Once that is obtained, you call the local inpatient psychiatric unit and obtain a bed for the patient. The patient is then sent to the inpatient unit via ambulance from your clinic. This process may take between two to four hours. As clinic time runs out, this may end up resulting in referral to the emergency room.

Refer the patient to the local emergency room: The patient should be safely transported there via ambulance. You place yourself at great risk if you identify patients as being suicidal and needing emergency care but allow them to seek it out or get there on their own. **Finally, please contact that ER and fax them your note.** It is the professional and courteous thing to do. In addition, your note and its history may make the difference between an admission versus inappropriate discharge resulting in an emergent patient call to you the next day or worse, a patient committing suicide.

If you have decided the patient needs emergency referral and he or she refuses care, a referral to the appropriate crisis line or mental health crisis team should be made. In more emergent situations, the police may be called (e.g., the patient tells you he is going home to "blow his brains out" with the gun he just purchased and leaves the clinic abruptly). You and your clinic are not an emergency room and you should not attempt to physically detain someone.





Violent or Potentially Violent Patients

Attempting to predict violence toward others is as difficult as predicting suicide. As with suicide, a past history of violence is a strong risk factor for future violence. Other risk factors include illicit drug and alcohol use (especially current intoxication), a history of criminal behavior, and a history of childhood abuse. In the clinic, you may encounter patients who are menacing, threatening, or overtly violent. You may also encounter patients who make threats about violence toward others in the course of a safe discussion with you and appropriate behavior in the clinic (much like a patient disclosing thoughts of suicide).

Patients Who Are Overtly Menacing, Threatening, or Violent in Clinic

Every clinic needs a plan for handling patients who present any threat to any provider, staff, or other patient in the clinic. In your clinic, what should a provider do if a patient hits him? What should front desk staff do if one patient threatens and assaults another patient in the waiting room? Who is ultimately in charge and responsible for documenting what occurred and following up with staff about improving future responses? Is there a chart mechanism for noting a patient history of inappropriate behavior in clinic?

This plan for dealing with serious violence and violent threats should include the following:

1. **Response Initiation.** What triggers the response to the threat or act of violence? Is there a panic button or alarm that is accessible in patient care areas? Any staff in the clinic should be able to initiate the response.
2. **Response.** Who will respond once the plan is initiated and who will be in charge? If security is available, they should be the first responders and the job of the clinic staff should be to avoid injury, keep others safe, and call police.
3. **Follow-up. Follow-up with staff is important.** Being threatened or assaulted can make individuals feel very frightened. It is worse when they do not feel supported or believe the clinic leaders are not addressing it or making sure it does not happen again. Legal follow-up will be necessary and difficult decisions regarding care will need to be made (will the patient ever be allowed back in the clinic and if not, where will that person go?).

Different clinicians have different levels of comfort when it comes to de-escalating a potentially violent situation. The safest response is to be clear that the patient is acting inappropriately and ask him to leave. In most situations, security should be contacted so the patient understands that you will neither respond to the threats aggressively nor allow him to continue acting in that way. The end result, at least, is the patient leaving the clinic that day and not returning until he can act appropriately.





Patients Reporting Violent Ideation or Threats of Future Violence

Approaching violent ideation is similar to approaching thoughts of suicide. A clinic protocol should include rules for screening, plans for gathering more information to make a decision about risk and the duty to warn, and a plan for further care.

Step 1: Screening

Asking about violent ideation is a standard part of the mental status exam. It should be asked of all new patients and those who may be at higher risk for violence (the intoxicated, psychotic, or agitated). One question could be:

“Have you been having any thoughts or desires to harm anyone?”

Step 2: Gathering More Information

If a patient reports thoughts of harming others, obtain more information including the presence of a plan, the means to carry out the plan, and a past history of violence toward others. Questions could include:

1. ***Do you have a specific plan to harm someone?***
2. ***Who are you planning to harm? Why?*** It will be vital to know if there is an identifiable victim. A patient who describes a clear and identifiable victim will likely need to be referred for emergency evaluation and authorities should be addressed to discharge the “duty to warn.”
3. ***Have you ever been violent toward someone before?*** This should include questions about arrests for assault, the type of assault (was there a weapon involved), and the role of alcohol or other drugs.

Step 3: Making a Treatment Decision

If the patient’s thoughts of harming someone else are accompanied by a genuine plan and an identifiable victim, you are left with a duty to protect the victim and find some type of treatment for your patient. Treatment planning should ideally involve your team and involve consideration of outpatient or inpatient treatment or emergency evaluation.

The Duty to Warn

Tarasoff v. The Regents of the University of California is the basis of our duty to warn laws. Tatiana Tarasoff, a young college student at UC Berkeley, was murdered by a male student with a mental illness who had told his therapist he planned to kill Ms. Tarasoff. The therapist had not warned Ms. Tarasoff or her family about this threat (although he had obtained inpatient treatment for the patient).

The law is straightforward. If a patient tells you he or she is going to hurt someone (and that someone is identifiable, not just a vague “somebody”) you have a duty to protect that potential victim. At the point the threat is divulged, privacy laws related to that matter are no longer relevant. As Justice Mathew O. Tobriner stated in the majority opinion of the CA Supreme Court: “the confidential character of patient-psychotherapist communications must yield to the extent that disclosure is essential to avert danger to others. The protective privilege ends where the public peril begins.”





There are a number of ways to discharge the duty to warn:

1. Contact the identifiable victim and disclose the threat.
2. Contact the police and disclose the threat (you will be asked the potential victim's name and address as well as that of the patient).
3. Ensure the safety of your patient and the victim through hospitalization of the patient (or in the case of the primary care clinic, emergency evaluation).

Depending on the circumstance, you may have to do one of these or all three. For instance, a patient with psychopathy and a history of violence might be best handled through emergency evaluation, contacting police, and contacting the potential victim. In other instances (such as a patient with schizophrenia with no history of violence who is having command hallucinations to hit his caregiver), the most important step is hospitalization and discussion with the caregiver, while contacting police is probably not needed. Consulting with the BHP and/or CP can help a team make the best informed decision.





Example Safety Protocol

This is an example safety protocol that can be adapted to your clinical setting, posted and/or available in print form for staff members to easily access when needed.

A patient threatens suicide



Ask the patient if s/he has a suicide plan



If the patient has a **credible plan** or is evasive in his/her answer



See Credible Plan Questions



Tell the patient that his/her suicidality is taken seriously and that s/he will be sent to the ED for emergent psychiatric evaluation



Notify the charge nurse and have a staff member sit with the patient while ambulance is called



A staff member needs to be with the patient at all times while waiting for the ambulance



Ambulance arrives and takes the patient to the ED



If the patient leaves the clinic against medical advice, call 911



The clinician or the nursing staff calls the ED and notifies the pending arrival of the patient and shares history.



Plan for follow-up to coordinate care



Enter a brief note in EMR documenting the reason for sending the patient to the ED (Do not dictate this note)



Plan for follow-up to coordinate care

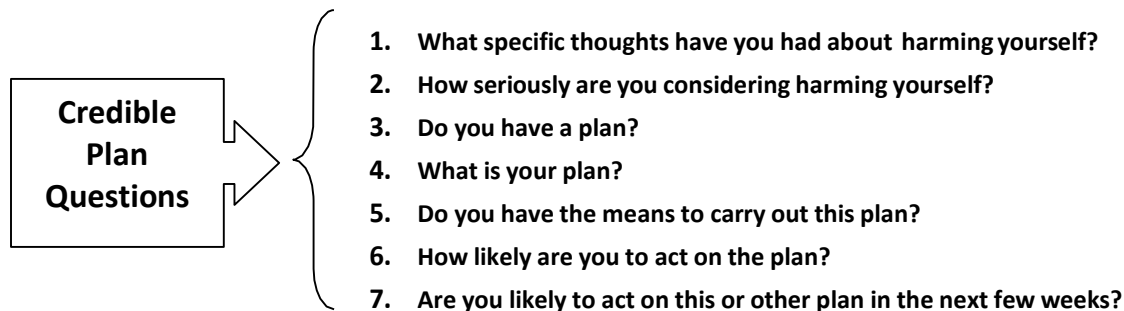




Credible Plan Questions

Most individuals who make statements suggestive of suicidal/self-harm ideation should be assessed further by a mental health professional for risk for suicide, psychiatric diagnosis, and appropriate treatment. **The issue is whether the assessment should be performed within the same day or less emergently.**

The evaluation of suicidal risk involves assessing multiple risk factors, including alcohol/drug dependence/abuse, prior suicide attempts, affective disorder, lack of support system, poor physical health, and hopelessness. After someone makes a suicidal statement or statements with clues about possible suicidal thinking, **some of the most useful questions that can be asked**



Other questions that can be helpful to ask in assessing risk

8. Do you have any hope for yourself?
9. Are you using drugs or alcohol to excess now?
10. Have you used drugs or alcohol to excess in the past?
11. Have you ever tried to kill or harm yourself in the past? If so, when and how?
12. Have any family members tried to kill themselves?
13. Do you have other people that you are closely connected to? Do you feel supported by these people?
14. Have you had serious depressions or other mental health problems in the past?

Risk Level

Low risk: no immediate plan to kill self, few risk factors, good physical health, support system

Moderate risk: no immediate plan to kill self but has several risk factors (prior suicide attempts, depressive disorder, substance abuse) or acute physical or psychosocial stressors (e.g., poor health, lack of support system, loss of spouse)

High risk: participant plans to kill self in immediate future, recently attempted suicide with lethal means, and clinician impression of carrying out suicide intent is strong due to one or more high-risk factors (e.g., prior suicide attempts [especially if recent], severe depression, active substance abuse, lack of support system, loss of spouse, feelings of hopelessness, poor health)





If a patient with safety concerns is not going to be hospitalized, then it is especially important to develop a good safety plan. Consider using national resources such as the safety plan below adapted from The National Suicide Prevention Lifeline: <http://www.suicidepreventionlifeline.org/>

Patient Safety Plan Template

Step 1: What to watch for that a crisis may be developing (thoughts, images, mood, situation, behavior):

1. _____
2. _____
3. _____

Step 2: Coping strategies—What I can do by myself do to take my mind off my problems (relaxation technique, physical activity):

1. _____
2. _____
3. _____

Step 3: Places and community (friend, family, neighbor, a coffee shop, a movie theater, a store) that provide distraction:

1. Name _____ Phone _____
2. Name _____ Phone _____
3. Place _____
4. Place _____

Step 4: Who can I ask for help:

1. Name _____ Phone _____
2. Name _____ Phone _____
3. Name _____ Phone _____

Step 5: Providers and resources I can contact during a crisis:

1. Clinician Name _____ Phone _____ Clinician Pager or Emergency Contact # _____
2. Clinician Name _____ Phone _____ Clinician Pager or Emergency Contact # _____
3. Local Urgent Care Services _____
Urgent Care Services Address _____
Urgent Care Services Phone _____
4. National Suicide Prevention Lifeline Phone: 1-800-273-TALK (8255)

Step 6: How I can make my environment safe:

1. _____
2. _____

The one thing that is most important to me and worth living for is:

Adapted from Safety Plan Template ©2008 Barbara Stanley and Gregory K. Brown





Care Manager Job Description & Summary of Responsibilities

The Care Manager is a core member of a Collaborative Care team, which includes the patient's primary care provider, a psychiatric consultant, and other mental health providers available in the primary care clinic. The Care Manager is responsible for coordinating and supporting mental health care within the clinic and for coordinating referrals to clinically indicated services outside the clinic. The Care Manager may provide evidence-based treatments or work with other mental health providers when such treatment is indicated.

Sometimes the care manager role is split or shared between a licensed professional and a paraprofessional (typically a medical assistant, community health specialist, or similar paraprofessional). The paraprofessional performs the majority of the care manager tasks (except those that are out of their scope of practice, like psychotherapy) and the licensed provider performs the remaining tasks.

DUTIES AND RESPONSIBILITIES

1. Support and closely coordinate mental health care with the patient's primary care provider and other treating mental health providers.
2. Screen and assess patients for common mental health and substance abuse disorders.
3. Provide patient education about common mental health and substance abuse disorders and available treatment options.
4. Monitor patients (in person or by telephone) for changes in clinical symptoms and treatment side effects or complications.
5. Support psychotropic medication management prescribed by PCPs, focusing on treatment adherence, side effects and other complications, and effectiveness of treatment.
6. Provide brief evidence-based psychotherapy such as Behavioral Activation, Problem-Solving Treatment, Motivational Interviewing, or other treatments appropriate for primary care settings.
7. Provide or facilitate in-clinic or outside referrals to evidence-based psychosocial treatments (e.g., CBT) as clinically indicated.
8. Participate in regularly scheduled (usually weekly) caseload consultation with the psychiatric consultant and communicate resulting treatment recommendations to the patient's PCP. Consultations will focus on patients new to treatment or who are not improving as expected.
9. Support patient engagement and follow-up in care.
10. Track patient follow-up and clinical outcomes using a registry. Document in-person and telephone encounters in the registry and use the system to identify patients that might be "falling through the cracks" and re-engage these patients.
11. Document patient progress and treatment recommendations in the registry to facilitate communication with PCPs, the psychiatric consultant, and other treating providers.
12. Facilitate treatment plan changes for patients who are not improving as expected in consultation with the PCP and the psychiatric consultant. These may include changes in medications or psychosocial treatments or appropriate referrals for additional services.
13. Facilitate referrals for clinically indicated services outside the primary care clinic (e.g., social services such as housing assistance, vocational rehabilitation, mental health specialty care, substance abuse treatment).
14. Complete relapse prevention plan with patients who are in remission.





Psychiatric Consultant Job Description & Summary of Responsibilities

Collaborative Care is an evidence-based and team-based model of collaborative integrated care in which primary care providers are supported by clinic-based behavioral health care managers (CMs) and Psychiatric consultants. All patients in the program have a designated PCP and a CM. The CM supports and tracks a caseload of patients. The psychiatric consultant is responsible for supporting mental health care provided by PCPs and CMs in the participating primary care clinics as well as providing direct patient consultations.

DUTIES AND RESPONSIBILITIES FOR PSYCHIATRIC CONSULTANTS

1. Conduct Regular Caseload Reviews with Care Manager

Conduct a regular (usually weekly) meeting with the clinic-based care manager (CM) to review patients who are new to treatment, who are not improving as expected, who present diagnostic or therapeutic challenges, or for whom the PCP has requested a psychiatric consultation.

2. Provide Consultations and Treatment Recommendations for Primary Care Providers (PCPs)

Provide diagnostic or treatment recommendations on patients reviewed with the care manager and communicate these recommendations to the PCP directly or through the patient's CM. These recommendations may include:

- a. Diagnostic recommendations
- b. Therapeutic recommendations involving pharmacological or non-pharmacological treatments or changes in treatment
- c. A direct consultation by the psychiatric consultant at the primary care clinic
- d. Ongoing management by the psychiatric consultant at the primary care clinic in close coordination with the patient's PCP
- e. Referral to additional behavioral health or social services and advice on treatment plans until patients are engaged in such care

Direct consultation, evaluation, and management of patients by the psychiatric consultant should focus on patients with diagnostic or therapeutic challenges identified by PCPs or CMs (e.g., complex pharmacological management; questions about bipolar disorder, psychosis, or suicidal ideation). Such direct consultations should be scheduled after review of the case with the patient's CM, who will usually have seen the patient for an initial visit and consulted with the PCP. They can be provided in person or via telemedicine (video or telephone) with or without the CM present, and they should be documented in the patient's medical record and billed as clinically appropriate.

3. Review Patient Progress and Document Recommendations

Use the registry to review patient progress and document recommendations for treatment and/or referrals within 24 hours of reviewing a case with a CM so that the recommendations can be easily shared with PCPs and other treating providers.

4. Communicate Limitations of Case Reviews and Consultations as Appropriate

Clearly communicate to CMs and PCPs the limitations of case reviews and consultations performed and treatment recommendations. If the case was reviewed with the CM and/or PCP but the psychiatrist did not evaluate the client in person, include the following statement in your consult note/recommendation:

"The above treatment considerations and suggestions are based on consultation with the patient's care manager and/or PCP and a review of information available in the shared registry and the patient's Electronic Health Record (EHR). I have not personally examined the patient. All recommendations should be implemented with consideration of the patient's relevant prior history and current clinical status. Please feel free to call me with any questions about the care of this patient."

5. Maintain Availability to Clinic Providers

- a. Maintain professional cell phone and e-mail accounts for contact during usual business hours.
- b. Respond to telephone calls from primary care providers and CMs within one business day. Respond to urgent telephone calls within one hour.
- c. Check professional e-mail account daily. Respond to e-mail questions/consultations within one business days, sooner if urgent.
- d. Coordinate with other Collaborative Care psychiatric consultants for vacation coverage and communicate these coverage arrangements to clinic providers and clinic staff.

6. Protect Patient Health Information

Ensure that all protected health information (PHI) in local computer/networks is stored in compliance with organization and HIPAA regulations.

7. Support Medication Management

Psychiatric consultants will not prescribe medications for patients whom they have not personally evaluated.

In general, they will also not prescribe medications in cases where they are performing a one-time consultation for the PCP and for whom the PCP continues as the primary treating provider, but they may make recommendations for medication management to the PCP. Psychiatric consultants who have evaluated a patient in person may provide short-term prescriptions in urgent situations (e.g., a change in medication is needed urgently) in consultation with the PCP.

Psychiatric consultants may provide ongoing medication management/prescriptions for a limited number of clinic patients in whom they are assuming ongoing medication management responsibility after discussion with and in coordination with the patient's PCP.

8. Participate in Quality Improvement Activities:

Meet regularly (monthly or at a minimum quarterly) with clinic-based CMs, PCPs, and clinic leadership to track and oversee Collaborative Care patient panels and aggregate clinical outcomes as summarized by registry reports. Suggest and help implement clinical and operational program improvements as appropriate.

9. Participate in Program Oversight

Participate in the monthly Collaborative Care Psychiatric Consultant meeting.

TYPICAL WORKLOAD

A typical assignment for a psychiatric consultants includes 20 % time (8 hours/week) and includes the following activities:

1. Caseload-focused review/consultation: 2-3 hours/designated CM*/week

This includes regular (weekly) consultation with the assigned CC, preparation for consultation, review of available medical records (e.g., PCP notes) and documentation of recommendations in registry or HER as instructed. This may also include direct communication about patients with PCPs.

** A full time CM may have an active caseload of 50 – 100 patients depending on the type of patients with safety-net patient panels usually followed on smaller caseloads.*

2. Direct patient consultation: 4-5 hours/week

This includes scheduled patient consults (new evaluations or follow-up visits), documentation of the encounter in the patient's medical record, communication of recommendations to the patient's CM and PCP, and support of billing activities for the in person visits performed.

3. Participation in program coordination, quality improvement, and training activities: approximately 1 hour/week.

This includes regular meetings focused on clinic-based and Collaborative Care QI activities (#s 8 and 9 above). It may also involve training of clinic-based or other Collaborative Care providers, support of trainees assigned to the clinic, or such activities as self-study and professional development relevant to Collaborative Care.

OPTIONAL ACTIVITIES

Training and Technical Assistance Activities:

Psychiatric consultants may participate in the development of training materials or participation in clinic-based or regional training meetings, webinars, or other training activities coordinated. They may also provide training and/or supervision to trainees (e.g., primary care or psychiatry residents) assigned at the participating primary care clinics as negotiated with clinic leadership and program leadership.

REQUIREMENTS

- Licensed psychiatrist, appointed and credentialed.
- Demonstrated ability to collaborate effectively in a team setting.
- Excellent communication skills.
- Positive, flexible, and solution-focused attitude.
- Ability to multitask during consultations.
- Ability to quickly synthesize medical and psychiatric data and formulate effective and evidence-based clinical recommendations.
- Interest in longitudinal follow-up of patients with diagnostic clarification and treatment intensification as needed to treat patients to symptom remission and to achieve individual treatment goals
- Basic (or better) typing skills.
- Intermediate (or better) computer skills (including file management, web-searching, web-page navigation, cut/paste, drag and drop, use of shortcuts and menus, and switching between windows).

DESIRED

- Board-eligible in psychiatry.
- Experience with primary care psychiatry, consultation-liaison psychiatry, or geriatric psychiatry.
- Experience working with patient populations that have clinical co-morbidities (e.g., co-occurring mental health, substance abuse, physical health, and chronic pain problems).





Screeners

Adult ADHD Self-Report Scale V1.1 (ASRS v1.1)

ADHD

<http://www.hcp.med.harvard.edu/ncs/asrs.php>

Alcohol Use Disorders Identification Test (AUDIT-C)

Substance use, alcohol, stimulants, opioids

http://www.integration.samhsa.gov/images/res/tool_auditc.pdf

Child Behavior Check List (CBCL)

ADHD

<http://www.aseba.org/forms/schoolagecbcl.pdf> (purchase required)

Clinical Institute Withdrawal Assessment of Alcohol Scale (revised) (CIWA-Ar)

Substance use, alcohol, stimulants, opioids

<http://www.mdcalc.com/ciwa-ar-for-alcohol-withdrawal/>

Composite International Diagnostic Interview (CIDI-3)

Mood disorders, bipolar; Mood disorders, depression

http://www.cqaimh.org/pdf/tool_cidi.pdf

Confusion Assessment Method (CAM)

Mood disorders, depression; Psychotic disorders

<https://www.healthcare.uiowa.edu/igec/tools/cognitive/CAM.pdf>

Conjoint Questionnaire for Alcohol and Other Drug Abuse (CAGE-AID)

Substance use, alcohol, stimulants, opioids

<http://www.agencymeddirectors.wa.gov/Files/cageover.pdf>

Drug Abuse Screening Test (DAST)

Substance use, alcohol, stimulants, opioids

<http://www.integration.samhsa.gov/clinical-practice/screening-tools#drugs>

Generalized Anxiety Disorder (GAD-7)

Anxiety disorders

<http://www.phqscreeners.com/>

Mini-Mental State Examination (MMSE)

Psychotic disorders

<http://www4.parinc.com/Products/Product.aspx?ProductID=MMSE-2> (purchase required)

Montreal Cognitive Assessment (MoCA)

Psychotic disorders

<http://www.mocatest.org/>

Pain Intensity and Opioid Interference Risk, Three-item scale assessment tool (PEG three-item scale)

Chronic pain

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2686775/pdf/11606_2009_Article_981.pdf

Patient Health Questionnaire (PHQ-2, PHQ-9, PHQ-15)

Mood disorders, depression

<http://www.phqscreeners.com/>

PTSD Checklist - civilian version (PCL-C)

Trauma disorders

http://www.mirecc.va.gov/docs/visn6/3_PTSD_CheckList_and_Scoring.pdf

UCLA PTSD Index Trauma Screen (UCLA PTSD Index)

Trauma disorders

<http://www.ptsd.va.gov/professional/assessment/child/ucla-ptsd-dsm-iv.asp> (purchase required)

Social Communication Questionnaire (SCQ)

Autism Spectrum Disorders

<http://www.wpspublish.com/store/p/2954/social-communication-questionnaire-scq> (purchase required)

Yale Obsessive Compulsive Checklist (Y-BOC)

Anxiety disorders

<http://www.adaa.org/screening-obsessive-compulsive-disorder-ocd>

Evidence-Based Psychopharmacology for the Collaborative Care Team

ANTIDEPRESSANT MEDICATIONS

AMITRIPTYLINE (ELAVIL)

DOSING INFORMATION: *Initiation for depression:* Week 1: Baseline EKG (if any history of cardiac disease, history of arrhythmias, or over 65 y/o), pulse, HR, weight. Consider BMP for baseline sodium in older adults. **Start:** 25-50 mg qHS (10-25 mg qHS in the elderly). Week 2 and beyond: Increase dose by 25-50 mg (10-25 mg in the elderly) per day each week, if tolerated, to an **Initial Target Dose** of 75 mg qHS (50 mg qHS in the elderly). **Typical Dosage Range:** 75-150 mg/day (50-100 mg qHS in the elderly). **Max Dose:** 300 mg/day (150 mg qHS in the elderly). *Initiation for insomnia (off-label):* Start 10 mg qHS; increase in 10-25 mg qHS increments, if tolerated; **Typical Dosage Range:** 10-50 mg qHS. *Initiation for pain (off-label):* Start 10 mg qHS; increase in 10-25 mg qHS increments; **Typical Dosage Range:** 10-50 mg qHS. **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: EKG (pretreatment, initial, and annual—if any history of cardiac disease, history of arrhythmias or over 65 y/o), pulse, HR, weight. Consider posttreatment BMP to rule out hyponatremia in older adults. Blood test for serum level available with defined therapeutic range (amitriptyline + nortriptyline): 100-250 ng/ml; Toxic: >500 ng/ml. Blood draw timed to achieve a trough level.

GENERAL INFORMATION: **Mechanism of Action:** TCA: serotonin > NE reuptake inhibitor. **FDA Indications:** Depression. **Off-Label Indications:** pain (doses up to 100 mg); second-line RX for PTSD. **Pharmacokinetics:** T_{1/2}: 9-27 hrs. **Common Side Effects (MDD):** Sedation, anticholinergic side effects (blurred vision, urinary retention, dry mouth, constipation—more so than nortriptyline); orthostatic hypotension, weight gain, sexual side effects, headache. **Black Box Warning:** Increased SI in patients <25 y/o. **Contraindications:** Known hypersensitivity reaction to the product, use of a MAOI within 14 days of stopping Elavil, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Elavil within 14 days of stopping a MAOI, use with cisapride due to the potential for increased QT interval and increased risk for arrhythmia, or use during the acute recovery period after a MI. **Warnings and Precautions:** Clinical worsening and suicide risk, highly lethal in overdose, serotonin syndrome, orthostatic hypotension, cardiac dysrhythmia, QTc prolongation, seizures, manic switch, hepatic changes, decreased blood cell count, hyperthermia, increased intraocular pressure, urinary retention, SIADH. **Metabolism/Pharmacogenomics:** Metabolized by 2D6 to less active metabolites and by 2C19 to nortriptyline. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Use caution with strong 2D6 inhibitors (e.g., fluoxetine and paroxetine), and with medications that affect QTc; check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk/Use Caution. **Dosage Form:** Tablet. **Generic available:** Yes. **Cost:** ⬇️. **FDA label from dailymed.nlm.nih.gov, Rev. 10.12.**

BUPROPION (WELLBUTRIN, FORFIVO, APLENZIN, ZYBAN)

DOSING INFORMATION: *Wellbutrin-IR:* Week 1: Baseline blood pressure. Consider BMP for baseline sodium in older adults. **Start IR:** 100 mg bid. Week 2: Increase to 100 mg tid, if tolerated (single dose should not exceed 150 mg). *Wellbutrin-SR:* Week 1: Baseline blood pressure: **Start SR:** 150 mg qAM. Week 2: Increase to an **Initial Target Dose** of 150 mg bid, if tolerated. *Wellbutrin-XL:* Week 1: Baseline blood pressure. **Start XL:** 150 mg qAM. Week 2: Increase to 300 mg qAM, if tolerated. **Note:** Aplenzin has a different titration. **Typical Dosage Range:** 300-450 mg/day. **Max Dose:** 400-450 mg qday. **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize risk of relapse.

MONITORING: Blood pressure. Consider posttreatment BMP to rule out hyponatremia in older adults. Reports of false-positive urine immunoassay screening tests for amphetamines have been reported in patients taking bupropion, consult lab if needed.

GENERAL INFORMATION: Wellbutrin has a novel mechanism of action (weak dopamine and NE reuptake inhibitor; stimulant like effect). **FDA Indications:** Major depressive disorder, season affective disorder (prophylaxis), and smoking cessation. **Off-Label Indications:** Second line RX for ADHD. **Pharmacokinetics:** T_{1/2} = 21 hr. **Common Side effects (XL-MDD):** Headache (34%), dry mouth (26%), >5 lb. weight loss (23%), insomnia (20%), nausea (13%), constipation (9%), anxiety (7%), flatulence (6%). **Black Box Warning:** Increased SI in patients < 25 y/o. Increased risk of neuropsychiatric symptoms and suicidality in patients taking bupropion for smoking

cessation. **Contraindications:** Known hypersensitivity reaction to the product, seizure disorder, current or prior diagnosis of bulimia or anorexia nervosa, abrupt discontinuation of alcohol or benzodiazepines, use of a MAOI within 14 days of stopping Wellbutrin, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Wellbutrin within 14 days of stopping a MAOI. **Warnings and Precautions:** Clinical worsening and suicide risk, neuropsychiatric symptoms and suicide risk in smoking cessation treatment, increased risk of seizures, use in patients with a history of traumatic brain injury, potential for hepatotoxicity and hepatic impairment, increased agitation and insomnia, hypertension, altered appetite and weight, activation of psychosis or hypomanic/manic switch, potential for renal impairment, street value/abuse potential. **Pharmacogenetics:** Metabolized by 2B6. **Significant drug-drug interactions:** Inhibitor of 2D6; check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk/Use Caution. **Dosage Form:** Tablet (do not cut, crush or chew). **Generic available:** IR, SR, XL; Cost: \$. **FDA label information from Drugs @FDA for Wellbutrin XL dated 7.26.11.**

CITALOPRAM (CELEXA)

DOSING INFORMATION: Week 1: Baseline weight. Consider BMP for baseline sodium in older adults and baseline QTc in all patients. **Start:** 20 mg qday. Week 2: Increase dose to 40 mg qday, if tolerated. **Initial, Typical Target, and Maximum Dose** of 40 mg qday (Max dose = 20 mg qday if ≥ 60 y/o, hepatically impaired, a CYP2C19 poor metabolizer, or taking a CYP2C19 inhibitor). **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: Weight, consider posttreatment BMP to rule out hyponatremia in older adults and posttreatment QTc in all patients.

GENERAL INFORMATION: Mechanism of Action: Highly selective serotonin reuptake inhibitor. **FDA Indications:**

Depression. **Other Indications:** Anxiety disorders. **Pharmacokinetics:** $T_{1/2}$ = 35 hrs. **Common Side effects (MDD):**

Nausea (21%), dry mouth (20%), somnolence (18%), sexual side effects/ejaculatory dysfunction (6%). **Black Box**

Warning: Increased SI in patients < 25 y/o. **Contraindications:** Known hypersensitivity reaction to the product.

Use of a MAOI within 14 days of stopping Celexa, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Celexa within 14 days of stopping a MAOI. **Warnings and Precautions:** Clinical

worsening and suicide risk, QTc prolongation and torsades de pointes, activation of hypomania/mania, serotonin syndrome, discontinuation symptoms, abnormal bleeding, hyponatremia, seizures. It is recommended that citalopram should not be used in patients with congenital long QTc syndrome, bradycardia, hypokalemia or hypomagnesemia, recent acute myocardial infarction, or uncompensated heart failure or used in combination

with drugs that prolong the QTc. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk/Use Caution.

Metabolism/Pharmacogenomics: Primarily metabolized by 2C19 & 3A4 with 2D6 playing a less significant role. Use caution in 2C19 poor metabolizers and in patients taking 2C19 inhibitors (cimetidine). **Significant drug-drug**

interactions: Weak 2D6 inhibitor; check all drug-drug interactions before prescribing. **Dosage Form:** Oral solution,

Tablet. **Generic available:** Yes. **Cost:** €. **FDA label information from Drugs @FDA for Celexa dated 12.3.12.**

CLOMIPRAMINE (ANAFRANIL)

DOSING INFORMATION: Week 1: Baseline EKG (if any history of cardiac disease, history of arrhythmias, or over 65 y/o), pulse, HR, weight. Consider BMP for baseline sodium in older adults. **Start:** 25 mg qHS—should be given with food and dose may be divided to limit GI effects. Week 2: increase to 50 mg qHS. Week 3: increase to 75 mg qHS.

Week 4: increase dose to an **Initial Target Dose** of 100 mg qHS. **Max Dose:** 250 mg/day. **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: EKG (pretreatment, initial, and annual—if any history of cardiac disease, history of arrhythmias or

over 65 y/o), pulse, HR, weight. Consider posttreatment BMP to rule out hyponatremia in older adults. Blood test for serum level available with defined therapeutic range: 150-300 ng/ml; Toxic > 500 ng/ml. Blood draw timed to achieve a trough level.

GENERAL INFORMATION: Mechanism of Action: TCA: serotonin >> NE reuptake inhibitor. **FDA Indications:** OCD.

Off-Label Indications: Depression. **Pharmacokinetics:** $T_{1/2}$: 32 hr. **Common Side Effects (OCD):** dry mouth (84%),

somnolence (54%), dizziness (54%), tremor (54%), headache (52%), constipation (47%), ejaculation failure (42%),

fatigue (39%), nausea (33%), increased sweating (29%), dyspepsia (22%), libido change (20%), impotence (20%), weight gain (18%), nervousness (18%), abnormal vision (18%), micturition disorder (14%), increased appetite (11%), paresthesia (9%), memory impairment (9%), anxiety (9%), rash (8%), vomiting (7%), twitching (7%), flatulence (6%), impaired concentration (5%), depression (5%). **Black Box Warning:** increased SI in patients <25 y/o. **Contraindications:** Known hypersensitivity reaction to the product, Use of a MAOI within 14 days of stopping Anafranil, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Anafranil within 14 days of stopping a MAOI, use during the acute recovery period after a MI. **Warnings and Precautions:** Clinical worsening and suicide risk, highly lethal in overdose, activation of hypomania/mania, serotonin syndrome, seizures, orthostatic hypotension, caution in patients with known cardiovascular disease, neuropsychiatric symptoms, caution and monitoring in patients with liver disease, decreased blood cell count, hyperthermia, sexual dysfunction, weight gain, caution in patients with hyperthyroidism/thyroid supplementation, increased intraocular pressure, a history of narrow-angle glaucoma, urinary retention, with tumors of the adrenal medulla, or with impaired renal function, discontinuation syndrome. Potentially prolongs QTc so caution is advised in patients with cardiovascular disease. **Metabolism/Pharmacogenomics:** Metabolized by 2D6 to less active metabolites and by 2C19 to active metabolites. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** use with caution with 2D6 inhibitors (e.g., fluoxetine); check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk/Use Caution. **Dosage Form:** Capsule. **Generic available:** Yes. **Cost:** \$. **FDA label information from Drugs @FDA for Anafranil dated 10.26.12.**

DESIPRAMINE (NORPRAMIN)

DOSING INFORMATION: Week 1: Baseline EKG (if any history of cardiac disease, history of arrhythmias, or over 65 y/o), pulse, HR, weight. Consider BMP for baseline sodium in older adults. **Start:** 25-50 mg qday (10-25 mg in older adults); May be given at night. Week 2 and beyond: Increase dose by 25-50 mg per day each week to and **Initial Target Dose** of 100 mg (50 mg for older adults), if tolerated. **Typical Dosage Range:** 100-200 mg (50-100 mg for older adults), **Max Dose:** 300 mg (150 mg older adults). **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: EKG (pretreatment, initial, and annual—if any history of cardiac disease, history of arrhythmias or over 65 y/o), pulse, HR, weight. Consider posttreatment BMP to rule out hyponatremia in older adults. Blood test for serum level available with defined therapeutic range: 115-250 ng/ml; Toxic > 500 ng/ml. Blood draw timed to achieve a trough level.

GENERAL INFORMATION: Mechanism of Action: TCA: NE >> serotonin reuptake inhibitor. **FDA Indications:** Depression. **Off-Label Indications:** ADHD, neuropathic pain. **Pharmacokinetics:** T_{1/2} is highly variable with a mean of 30 hr. **Common Side effects (MDD):** Anticholinergic side effects (blurred vision, urinary retention, dry mouth, constipation—least of the group of TCAs), weight gain, GI upset, sexual side effects, somnolence, headache. **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Known hypersensitivity reaction to the product, use of a MAOI within 14 days of stopping Norpramin, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Norpramin within 14 days of stopping a MAOI, or use during the acute recovery period after a MI. **Warnings and Precautions:** Clinical worsening and suicide risk, highly lethal in overdose, activation of hypomania/mania, serotonin syndrome, orthostatic hypotension, QTc prolongation, hepatic changes, decreased blood cell count, hyperthermia, increased SIADH. Use with extreme caution in patients with cardiovascular disease, with a family history of sudden death, cardiac dysrhythmias, or cardiac conduction disturbances, with a history of urinary retention or glaucoma, with thyroid disease, or with a history of seizures. **Metabolism/Pharmacogenomics:** Metabolized by 2D6 and 2C19 (minor). Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** use with caution with 2D6 inhibitors (e.g., fluoxetine and paroxetine) and with medications that affect the QTc interval; Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk/Use Caution. **Dosage Form:** Tablet. **Generic available:** Yes. **Cost:** \$. **FDA label information from Drugs @FDA for Norpramin dated 11.19.2012.**

DESVENLAFAXINE (PRISTIQ)

DOSING INFORMATION: Week 1: Obtain blood pressure and weight. Consider BMP for baseline sodium in older

adults. **Start:** 50 mg qday. **Initial Target and Typical Dose:** 50 mg qday. **Max Dose:** No evidence of additional benefit for doses greater than 50 mg. **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: Blood pressure, weight. Consider posttreatment BMP to rule out hyponatremia in older adults.

GENERAL INFORMATION: Mechanism of Action: Serotonin/Norepinephrine Reuptake Inhibitor (SNRI). **FDA Indications:** MDD. **Off-Label Indications:** None. **Pharmacokinetics:** $T_{1/2}$ = 11 hr. **Common Side effects (MDD):** Nausea (22%), dizziness (13%), hyperhidrosis (10%), insomnia (9%), constipation (9%), decreased appetite (5%), specific male sexual function disorders (4%).

Black Box Warning: Increased SI in patients < 25 y/o. **Contraindications:** Known hypersensitivity reaction to the product, use of a MAOI within 7 days of stopping Pristiq, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Pristiq within 14 days of stopping a MAOI. **Warnings and Precautions:** Clinical worsening/suicide risk, serotonin symptoms or NMS, elevated blood pressure, abnormal bleeding, narrow angle glaucoma, hypomanic/manic switch, discontinuation syndrome, seizure, hyponatremia, interstitial lung disease and eosinophilic pneumonia. **Metabolism/Pharmacogenomics:** Primarily metabolized by conjugation. Minor metabolism by 3A4. **Significant drug-drug interactions:** Minimal; potential for abnormal bleeding with NSAIDs or anticoagulants; check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk /Not Recommended. **Dosage Form:** Tablet (Do not cut, crush or chew). **Generic available:** No. **Cost:** \$\$\$. **FDA label information from Drugs @FDA for Pristiq dated 12.23.13.**

DOXEPIN (SINEQUAN, SILENOR)

DOSING INFORMATION: Initiation for Anxiety and Depression (doxepin): Week 1: Baseline EKG (if any history of cardiac disease, history of arrhythmias, or over 65 y/o), pulse, HR, weight. Consider BMP for baseline sodium in older adults. **Start (doxepin):** 25-50 mg qHS (10-25 mg qHS in older adults). Week 2 and beyond: Increase dose by 25-50 mg qHS per day each week to an **Initial Target Dose** of 75 qHS (50 mg qHS for older adults), if tolerated. **Typical Dosage Range:** 75-150 mg qHS (50-100 mg qHS for older adults). **Max Dose:** 300 mg/day (up to 150 mg in single dose and a total of 150 mg/day in the elderly). **Initiation for Insomnia (Silenor):** 6 mg qHS (3 mg qHS for older adult). Can use Silenor or 10 mg capsule of doxepin dissolved in juice and use half ~5 mg. OF NOTE: Should not be taken within 3 hours of a meal. **Discontinuation** (for depression-anxiety): 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: EKG (pretreatment, initial, and annual—if any history of cardiac disease, history of arrhythmias or over 65 y/o), pulse, HR, weight. Consider posttreatment BMP to rule out hyponatremia in older adults.

GENERAL INFORMATION: Mechanism of Action: Sedating TCA: serotonin/NE reuptake inhibitor. **FDA Indications:** Depression and/or anxiety, insomnia. **Off-Label Indications:** Chronic pain, urticaria. **Pharmacokinetics:** $T_{1/2}$ = 6-8 hrs; major metabolite 24-52 hr. **Common Side effects (MDD):** Sedating and anticholinergic (blurred vision, urinary retention, dry mouth, constipation), orthostatic hypotension, weight gain, sexual side effects, headache. **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Known hypersensitivity reaction to the product, use of a MAOI within 14 days of stopping doxepin, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of doxepin within 14 days of stopping a MAOI, use in patients with glaucoma or a tendency to urinary retention. **Warnings and Precautions:** Clinical worsening and suicide risk, highly lethal in overdose, abnormal thinking and behavioral changes (e.g., sleep driving), serotonin syndrome, orthostatic hypotension, cardiac dysrhythmia, QTc prolongation, seizures, hypomanic/manic switch, hepatic changes, decreased blood cell count, hyperthermia, increased intraocular pressure, urinary retention, SIADH. **Metabolism/Pharmacogenomics:** Metabolized by 2D6 and 2C19 and to a lesser extent by 1A2 and 2C9. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Use caution with strong 2D6 inhibitors (e.g., fluoxetine and paroxetine) and medications that affect QTc; check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Contraindicated. **Dosage Form:** Capsule, Tablet (Silenor), Oral solution. **Generic available:** Yes; **Cost:** doxepin c, Silenor \$\$. **FDA label from dailymed.nlm.nih.gov, Rev. 10.07 (doxepin) and from Drugs @FDA 3.17.10 (Silenor).**

DULOXETINE (CYMBALTA)

DOSING INFORMATION: Week 1: Obtain blood pressure and weight. Consider BMP for baseline sodium in older

adults. **Start:** 30 mg qday. Week 2: Increase dose to the **Initial and Typical Target Dose** of 60 mg qday or 30 mg bid, if tolerated. **Max Dose:** 120 mg qday (little evidence that higher doses are beneficial). **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: Blood pressure, weight. Consider posttreatment BMP to rule out hyponatremia in older adults.

GENERAL INFORMATION: Mechanism of Action: Serotonin/Norepinephrine Reuptake Inhibitor (SNRI). **FDA**

Indications: MDD, GAD, diabetic peripheral neuropathic pain, fibromyalgia; chronic musculoskeletal pain. **Off-**

Label Indications: Second-line ADHD, other pain, other anxiety. **Pharmacokinetics:** $T_{1/2}$ = 12 hrs. **Common Side**

effects (MDD & GAD): nausea (25%), dry mouth (15%), diarrhea (10%), constipation (10%), fatigue (10%), dizziness (10%), somnolence (10%), insomnia (10%), decreased appetite (7%), hyperhidrosis (6%), vomiting (5%), agitation (5%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Known hypersensitivity

reaction to the product, use of a MAOI within 14 days of stopping Cymbalta, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Cymbalta within 14 days of stopping a MAOI, use in patients with uncontrolled narrow angle glaucoma. **Warnings and Precautions:** Suicidality, hepatotoxicity (should not be prescribed in patients with substantial alcohol use or evidence of chronic liver disease), orthostatic hypotension and syncope, serotonin syndrome, abnormal bleeding, severe skin reactions, discontinuation symptoms, manic switch, seizures, increased BP, use with 1A2 inhibitors or Thioridazine, hyponatremia, hepatic insufficiency and severe renal impairment, use caution in patient with controlled narrow-angle glaucoma and with slow gastric emptying, elevation in fasting blood glucose and HbA_{1c}, urinary hesitance and retention. **Metabolism/Pharmacogenomics:** Metabolized by 1A2 and 2D6. **Significant drug-drug interactions:** 2D6 inhibitor. Avoid co-administration with potent 1A2 inhibitors (e.g., fluvoxamine); and use cautiously with 2D6 inhibitors (e.g., Prozac). Potential for abnormal bleeding with NSAIDs or anticoagulants; Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk/Not Recommended. **Dosage Form:** Capsule (Do not cut, crush or chew). **Generic available:** Yes. **Cost:** \$\$ **FDA label information from Drugs @FDA for Cymbalta dated 10.18.2012.**

ESCITALOPRAM (LEXAPRO)

DOSING INFORMATION: Week 1: Baseline weight. Consider BMP for baseline sodium in older adults). **Start:** 5 mg qday. Week 2: Increase dose to an **Initial Target Dosage** of 10 mg qday, if tolerated. **Typical Dosage Range:** 10-20 mg qday. **Max:** 20 mg qday. **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: Weight. Consider posttreatment BMP to rule out hyponatremia in older adults.

GENERAL INFORMATION: Mechanism of Action: Highly selective serotonin reuptake inhibitor; S-enantiomer of the racemic derivative of citalopram. **FDA Indications:** MDD (acute and maintenance), GAD. **Off-Label Indications:**

Other anxiety disorders. **Pharmacokinetics:** $T_{1/2}$ = 27-32 hrs. **Common Side effects (MDD):** nausea (15%), ejaculation disorder (9%), insomnia (9%), somnolence (6%), fatigue (5%), sweating increased (5%). **Black Box**

Warning: Increased SI in patients < 25 y/o. **Contraindications:** Known hypersensitivity reaction to escitalopram or citalopram. Use of a MAOI within 14 days of stopping Lexapro, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Lexapro within 14 days of stopping a MAOI. Concomitant use with pimozone. **Warnings and Precautions:** Clinical worsening and suicide risk, serotonin syndrome, discontinuation symptoms, seizures, hypomanic/manic switch, hyponatremia, abnormal bleeding.

Metabolism/Pharmacogenomics: Primarily metabolized by 2C19 & 3A4. **Significant drug-drug interactions:** Weak 2D6 inhibitor; Use caution when coadministered with drugs metabolized by 2D6. Check all drug-drug interactions.

Pregnancy: Category C. **Breastfeeding:** Excreted in breast milk/Use Caution. **Dosage Form:** Oral solution, Tablet.

Generic available: Yes. **Cost:** €. **FDA label information from Drugs @FDA for Lexapro dated 12.3.12.**

FLUOXETINE (PROZAC, SARAFEM)

DOSING INFORMATION: Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start:** 10 mg qday. Week 2: Increase dose to an **Initial Target Dose** of 20 mg qday (for geriatric patients, a lower initial dose or longer dosing interval is recommended and in bulimia the initial target dosage is 60 mg qday), if tolerated. Week 4 and beyond: Consider further dose increases in 10-20 mg qday increments, as needed and tolerated. **Typical**

Dosage Range: 20-60 mg qday. **Max:** 80 mg qday. **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: Weight. Consider posttreatment BMP to rule out hyponatremia in older adults.

GENERAL INFORMATION: Mechanism of Action: Selective serotonin reuptake inhibitor. **FDA Indications:** MDD (acute and maintenance), OCD, panic disorder, bulimia nervosa, premenstrual dysphoric disorder. **Off-Label Indications:** Other anxiety, fibromyalgia. **Pharmacokinetics:** T_{1/2} parent = 4-6 days, active metabolite = 4-16 days. **Common Side effects MDD:** nausea (21%), insomnia (16%), nervousness (14%), somnolence (13%), anxiety (12%), diarrhea (12%), anorexia (11%), dry mouth (10%), tremor (10%), asthenia (9%), sweating (8%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Known hypersensitivity reaction to fluoxetine. Use of a MAOI within 5 weeks of stopping fluoxetine, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of fluoxetine within 5 weeks of stopping a MAOI. Do not use pimozide or Thioridazine with fluoxetine. **Warnings and Precautions:** Clinical worsening and suicide risk, increased suicidality, serotonin syndrome, allergic reactions and rash, manic switch, seizures, altered appetite and weight, abnormal bleeding, hyponatremia, anxiety and insomnia, QT prolongation, long half-life. **Metabolism/ Pharmacogenomics:** Primarily metabolized by 2D6. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Potent 2D6 inhibitor; Use significant caution when coadministered with drugs metabolized by 2D6 (e.g., TCAs). Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk /Not Recommended. **Dosage Form:** Oral solution, Capsule, Tablet. **Cost:** ¢ **Generic available:** Yes, Inexpensive. **FDA label information from Drugs @FDA for Prozac dated 7.26.2013.**

FLUVOXAMINE (LUVOX): IR—IMMEDIATE RELEASE, CR—SUSTAINED RELEASE

DOSING INFORMATION: Luvox IR: Week 1: Baseline weight. Consider BMP for baseline sodium in older adults.

Start IR: 50 mg qHS. Week 2: Increase to an **Initial Target Dose (IR)** of 100 mg qHS, if tolerated. Week 3-4 and beyond: Consider further increases in 50 mg increments qHS q3-4 weeks. **Luvox CR:** Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start CR:** 100 mg qHS, the **Initial Target Dose (CR)**. Week 3-4 and beyond: Consider further increases in 50 mg increments q3-4 weeks, if tolerated. **Typical Dosage Range (IR/CR):** 100 mg-200 mg qHS. **Max Dose:** 300 mg/day. **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: Weight. Consider posttreatment BMP to rule out hyponatremia in older adults.

GENERAL INFORMATION: Mechanism of Action: Selective serotonin reuptake inhibitor. **FDA Indications:** OCD. **Off-Label Indications:** Depression, other anxiety. **Pharmacokinetics:** T_{1/2} = 15-16 hr. **Common Side effects (OCD-IR):** Nausea (40%), somnolence (22%), insomnia (21%), asthenia (14%), dry mouth (14%), nervousness (12%), diarrhea (11%), dizziness (11%), dyspepsia (10%), abnormal ejaculation (8%), sweating (7%), anorexia (6%), vomiting (5%), tremor (5%), anxiety (5%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Known hypersensitivity reaction to fluvoxamine. Use of a MAOI within 14 days of stopping fluvoxamine, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of fluvoxamine within 14 days of stopping a MAOI. Coadministration of tizanidine, thioridazine, alosetron, pimozide, or ramelteon. **Warnings and Precautions:** Clinical worsening and suicide risk, serotonin syndrome, important drug-drug interactions (SEE CONTRAINDICATIONS and DRUG-DRUG INTERACTIONS), discontinuation symptoms, abnormal bleeding, hypomanic/manic switch, seizures, hyponatremia. **Metabolism/Pharmacogenomics:** Primarily metabolized by 2D6. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Use with great caution with other medications as fluvoxamine is a potent inhibitor of multiple P450 enzymes including 1A2, 2C9, 3A4, and 2C19 (SEE CONTRAINDICATIONS). Fluvoxamine is a relatively weak 2D6 inhibitor. Use with caution with 2D6 inhibitors; OF NOTE: tobacco induces the metabolism of Luvox—consider dosage adjustment when starting or stopping tobacco; Check all drug-drug interactions and **CONSIDER CONSULTATION WITH A PHARMACIST BEFORE PRESCRIBING THIS MEDICATION.** **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk/Use Caution. **Dosage Form:** Capsule (Do not cut, crush or chew), Tablet. **Generic available:** IR: Yes; CR: Yes. **Cost:** IR ¢, CR \$\$\$. **FDA label information from Drugs @FDA for Luvox dated 11.30.2012.**

IMIPRAMINE (TOFRANIL IR, TOFRANIL PM)

DOSING INFORMATION: Tofranil IR: Week 1: Baseline EKG (if any history of cardiac disease, history of

arrhythmias, or over 65 y/o), pulse, HR, weight. Consider BMP for baseline sodium in older adults. **Start IR:** 25-50 mg qHS (10-25 mg in older adults). Week 2 and beyond: Increase dose by 25-50 mg per day each week to **initial target dosage (IR)** of 75 mg qHS (50 mg in older adults), if tolerated. **Typical Dosage Range (IR):** 75-150 mg qHS (50-100 mg qHS in older adults). **Max (IR):** 300 mg (up to 150 mg in single dose and 150 mg max dose in older adults). **Tofranil-PM:** Week 1: Baseline EKG (if any history of cardiac disease, history of arrhythmias, or over 65 y/o), pulse, HR, weight. Consider BMP for baseline sodium in older adults. **Start PM:** 75 mg qHS, the **Initial Target Dose (PM)** (25-50 mg qHS in older adults—use Tofranil at these dosages). Week 4-6 and beyond: Increase dose in 25-50 mg per day increments as needed and tolerated. **Typical Dosage Range (PM):** 75-150 qHS. (50-100 mg qHS for older adults). **Max (PM):** 300 mg/day (150 mg in older adults). **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: EKG (pretreatment, initial, and annual—if any history of cardiac disease, history of arrhythmias or over 65 y/o), pulse, HR, weight. Consider posttreatment BMP to rule out hyponatremia in older adults. Blood test for serum level available with defined therapeutic range: 150-300 ng/ml; Toxic >500 ng/ml.

GENERAL INFORMATION: Mechanism of Action: TCA: serotonin > NE reuptake inhibitor. **FDA Indications:** Depression. **Off-Label Indications:** Second-line PTSD. **Pharmacokinetics:** $T_{1/2}$ = 8-20 hrs; desipramine (active metabolite) highly variable with a mean of 30 hr. **Common Side effects (MDD):** Anticholinergic (moderate in the group of TCAs), weight gain, GI upset, sexual side effects, somnolence, headache. **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Known hypersensitivity reaction to imipramine. Use of a MAOI within 14 days of stopping imipramine, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of imipramine within 14 days of stopping a MAOI. Acute recovery period after MI. **Warnings and Precautions:** Clinical worsening and suicide risk, highly lethal in overdose, serotonin syndrome, photosensitization, activation of psychosis, hypomanic/manic switch, orthostatic hypotension, QTc prolongation, hepatic changes, decreased blood cell count, hyperthermia, blood glucose dysregulation, increased intraocular pressure, urinary retention, narrow angle glaucoma, SIADH. Per FDA, use with extreme caution in patients with cardiovascular disease, with a history of urinary retention or glaucoma, with thyroid disease, with a history of seizures, or on clonidine or similar agents. Caution in patients with significant hepatic or renal disease.

Metabolism/Pharmacogenomics: Metabolized by 2D6 to less active metabolites and by 2C19 to desipramine. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Use caution with strong 2D6 inhibitors (e.g., fluoxetine and paroxetine), and with medications that affect QTc; check all drug-drug interactions.

Pregnancy: Category D. **Breastfeeding:** Excreted in breast milk/Use Caution. **Dosage Form:** Capsule, Tablet.

Generic available: Yes for both Tofranil and Tofranil-PM. Cost: Tofranil €, Tofranil-PM \$. **FDA label for Tofranil from dailymed.nlm.nih.gov, Rev. 9.2009. FDA label information from Drugs @FDA for Tofranil-PM dated 10.26.2012**

MIRTAZAPINE (REMERON)

DOSING INFORMATION: Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start:** 15 mg qHS (7.5 mg qHS in older adults). Week 2: Increase to an **Initial Target Dose** of 30 mg qHS (15 mg qHS in older adults), if tolerated. **Typical Dosage Range:** 30-45 mg qHS (15-30 mg qHS in older adults). **Max Dose:** 45 mg qHS (30 mg qHS in older adults). **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: Weight, lipids. Consider posttreatment BMP to rule out hyponatremia in older adults.

GENERAL INFORMATION: Mechanism of Action: Novel; central pre-synaptic α_2 -adrenergic antagonist effects, which results in increased release of norepinephrine and serotonin. **FDA Indications:** MDD. **Off-Label Indications:** Other anxiety, neuropathic pain, insomnia, anti-nausea effect (similar mechanism to ondansetron).

Pharmacokinetics: $T_{1/2}$ = 26 hrs (females), 37 hrs (males). **Common Side effects (MDD):** Somnolence (54%), dry mouth (25%), increased appetite (17%), constipation (13%), weight gain (12%), dizziness (7%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Known hypersensitivity reaction to mirtazapine. Use of a MAOI within 14 days of stopping mirtazapine, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of mirtazapine within 14 days of stopping a MAOI. **Warnings and Precautions:** Clinical worsening and suicide risk, serotonin syndrome, hypomanic/manic switch, agranulocytosis (avoid in immunocompromised), discontinuation symptoms, akathisia/psychomotor restlessness, hyponatremia, increased

cholesterol/triglycerides, dizziness, increased appetite/weight gain, transaminase elevations, seizures.

Metabolism/Pharmacogenomics: Metabolized by 1A2, 2D6, and 3A4. **Significant drug-drug interactions:** Use caution with potent 3A4 inhibitors (e.g., ketoconazole and protease inhibitors) and enzyme inducers (e.g., carbamazepine). Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk/Use Caution. **Dosage Form:** Orally Disintegrating Tablet, Tablet. **Generic available:** Yes. **Cost:** ¢. **FDA label information from Drugs @FDA for Remeron dated 10.30.2012.**

NORTRIPTYLINE (PAMELOR, AVENTYL)

DOSING INFORMATION: Week 1: Baseline EKG (if any history of cardiac disease, history of arrhythmias, or over 65 y/o), pulse, HR, weight. Consider BMP for baseline sodium in older adults. **Start:** 25 mg qHS (10 mg qHS in older adults). Week 2 and beyond: Increase dose by 25-50 mg qHS (10 mg qHS in older adults) each week to an **Initial Target Dose** of 75 mg qHS (30 mg qHS for older adults), if tolerated. **Typical Dosage Range:** 75-100 mg qHS (30-50 mg qHS in older adults). **Max Dose:** 150 mg qHS (75 mg qHS in older adults). **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: EKG (pretreatment, initial, and annual—if any history of cardiac disease, history of arrhythmias or over 65 y/o), pulse, HR, weight. Consider posttreatment BMP to rule out hyponatremia in older adults. Blood test for serum level available with defined therapeutic range: 50-150 ng/ml; toxic >500 ng/ml. The FDA recommends testing serum levels in adults in doses above 100 mg qHS. Blood draw timed to achieve a trough level.

GENERAL INFORMATION: Mechanism of Action: TCA: NE > serotonin reuptake inhibitor. Generally better tolerated than other TCAs. **FDA Indications:** Depression. **Off-Label Indications:** neuropathic pain (doses up to 75 mg). **Pharmacokinetics:** T_{1/2}: highly variable 16-90+ hr. **Common side effects (MDD):** Sedation, anticholinergic side effects (blurred vision, urinary retention, dry mouth, constipation), orthostatic hypotension, weight gain, nausea, headache, sexual side effects. **Black Box:** Increased SI in patients <25 y/o. **Contraindications:** Known hypersensitivity reaction to the product, use of a MAOI within 14 days of stopping Pamelor, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Pamelor within 14 days of stopping a MAOI, or use during the acute recovery period after a MI. **Warnings and Precautions:** Clinical worsening and suicide risk, highly lethal in overdose, hypomanic/manic switch, serotonin syndrome, orthostatic hypotension, QTc prolongation, hepatic changes, decreased blood cell count, hyperthermia, urinary retention, SIADH, use in patients with cardiovascular disease, who have glaucoma or a history of urinary retention, with a history seizures, or with hyperthyroidism; use with quinidine. **Metabolism/Pharmacogenomics:** Metabolized by 2D6 to less active metabolites. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** use caution with strong 2D6 inhibitors (e.g., fluoxetine), and with medications that affect QTc; check all drug-drug interactions.

Pregnancy: **Category D; associated w/ increased risk of teratogenesis (need to inform women of childbearing age of this risk).** **Breastfeeding:** Excreted in breast milk/Use Caution. **Dosage Form:** Capsules, Oral solution. **Generic available:** Yes. **Cost:** ¢. **FDA label information from Drugs @FDA for Pamelor dated 10.26.2012.**

PAROXETINE (PAXIL CR, PAXIL, PEXEVA): IR: PAXIL, PEXEVA; CR: SUSTAINED RELEASE

DOSING INFORMATION: Paxil IR: Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start IR:** 10 mg qday. Week 2: Increase to an **Initial Target Dose (IR)** of 20 mg qday (40 mg qday for OCD), if tolerated. Week 4 and beyond: Consider further increases as needed in 10 mg qday per week increments as tolerated. **Typical Dosage Range (IR): 20-60 mg qday. Max Dose (IR): 60 mg qday.** Paxil CR: Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start CR:** 25 mg qday (the **Initial Target Dose**). Week 4 and beyond: Consider further increases as needed in 12.5 mg qday per week increments. **Usual Dosage Range (CR): 25-62.5 mg qday. Max Dose (CR): 62.5 mg qday. Discontinuation:** *Often problematic.* 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: Weight. Consider posttreatment BMP to rule out hyponatremia in older adults.

GENERAL INFORMATION: Mechanism of Action: Potent selective serotonin reuptake inhibitor, which is quite anticholinergic. **FDA Indications:** GAD, MDD, OCD, Panic Disorder, PTSD, PMDD, Social Phobia. **Pharmacokinetics:** T_{1/2} = 21 hrs. **Common Side effects (MDD-IR):** Nausea (26%), somnolence (23%), dry mouth (18%), asthenia (15%), constipation (14%), dizziness (13%), insomnia (13%), sexual side effects (13%), diarrhea (12%), tremor (8%), decreased appetite (6%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Known

hypersensitivity reaction to Paxil. Use of a MAOI within 4 weeks of stopping Paxil, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Paxil within 4 weeks of stopping a MAOI. Concomitant use with pimozide or thioridazine. **Warnings and Precautions:** Clinical worsening and suicide risk, serotonin syndrome, hypomanic/manic switch, teratogenic effects, seizures, discontinuation syndrome, drug-drug interactions, use with tamoxifen, akathisia, abnormal bleeding, hyponatremia, bone fracture.

Metabolism/Pharmacogenomics: Metabolized by 2D6. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Strong 2D6 inhibitor. Use caution with drugs metabolized by 2D6 (e.g., TCAs); check all drug-drug interactions. **Pregnancy:** **Category D; associated w/ increased risk of teratogenesis (need to inform women of childbearing age of this risk).** **Breastfeeding:** Excreted in breast milk/Use Caution. **Dosage Form:** Oral solution, Tablet, Coated Tablet (Do not cut, crush or chew). **Generic available:** IR: Yes; CR: yes, Cost: IR **¢**; CR **\$**. **FDA label information from Drugs @FDA for Paxil dated 12.18.2012.**

SERTRALINE (ZOLOFT)

DOSING INFORMATION: Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start:** 25 mg qday. Week 2: Increase to an **Initial Target Dose** of 50 mg qday, if tolerated. Week 4 and beyond: Consider further increases in dose if needed and tolerated, in 25 mg qday per week increments. **Typical Dosage Range: 50-200 mg qday. Max Dose:** 200 mg qday. **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: Weight. Consider posttreatment BMP to rule out hyponatremia in older adults. OF NOTE: false-positive urine immunoassay screening tests for benzodiazepines have been reported in patients taking sertraline.

GENERAL INFORMATION: Mechanism of Action: Selective serotonin reuptake inhibitor. **FDA Indications:** MDD, OCD, panic disorder, PTSD, social phobia, PMDD. **Off-Label Indications:** Other anxiety. **Pharmacokinetics:** T_{1/2} = 26 hrs. **Common Side effects (MDD):** Nausea (26%), diarrhea (18%), dry mouth (16%), insomnia (16%), somnolence (13%), dizziness (12%), tremor (11%), fatigue (11%), increased sweating, (8%), ejaculation failure (7%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Known hypersensitivity reaction to Zoloft. Use of a MAOI within 4 weeks of stopping Zoloft, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Zoloft within 4 weeks of stopping a MAOI. Concomitant use with pimozide. **Warnings and Precautions:** Clinical worsening and suicide risk, hypomanic/manic switch, serotonin symptoms, weight loss, seizure, discontinuation symptoms, abnormal bleeding, altered platelet function, hyponatremia, weak uricosuric effect, angle closure glaucoma. **Metabolism/Pharmacogenomics:** Metabolized by multiple P450 enzymes with 2C19 having the greatest pharmacogenetic and drug-drug interaction evidence. Use caution with 2C19 poor metabolizers. **Significant drug-drug interactions:** Weak 2D6 inhibitor. Use caution with drugs metabolized by 2D6 (e.g., TCAs); check all drug-drug interactions. **Pregnancy:** Category C. **Breastfeeding:** Compatible. **Dosage Form:** Oral solution, Tablet. **Generic available:** Yes. **Cost:** **¢**. **FDA label information from Drugs @FDA for Zoloft dated 2.1.2013.**

TRAZODONE (DESYREL [IR], OLEPTRO [ER]) **DOSING INFORMATION: Initiation for Depression: Trazodone IR:** Week 1: Baseline blood pressure, weight. Consider BMP for baseline sodium in older adults. **Start IR:** 25-50 mg bid-tid; increase by 25-50 mg/day per week, if tolerated, to an **Initial Target Dose (IR)** of 150 mg/day. Week 4 and beyond: Consider further increases in dose as needed and tolerated in 25-50 mg/day per week increments. **Typical Dosage Range (IR):** 150-300 mg/day. **Max Dose (IR):** 400 mg/day. **Oleptro (ER):** Week 1: Baseline blood pressure, weight. Consider BMP for baseline sodium in older adults. **Start ER:** 150 mg qHS (the **Initial Target Dose**). Week 4 and beyond: Can consider further increases in 75 mg/day per week increments. **Typical Dosage Range of 150-300 mg qHS. Max Dose Oleptro:** 375 mg qHS. **Initiation for insomnia (off-label):** **Start:** 25-50 mg qHS (the initial target dose); increase in 25-50 mg qHS per week increments, if tolerated; typical dose 50-200 mg qHS. **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: Weight; Consider posttreatment BMP to rule out hyponatremia in older adults. Monitor for orthostatic hypotension in elderly and other vulnerable populations.

GENERAL INFORMATION: Mechanism of Action: Serotonin reuptake inhibitor. **FDA Indications:** Depression. **Other Indications:** Insomnia, depression augmentation. **Pharmacokinetics:** T_{1/2} = 10 hrs. **Common Side effects**

(MDD-trazodone): Drowsiness (41%), dry mouth (34%), dizziness/lightheadedness (28%), headache (20%), blurred vision (15%), nausea/vomiting (13%), constipation (8%), skin condition/edema (5%), fatigue (6%), weight loss (6%), diarrhea (5%), musculoskeletal aches/pains (5%), tremors (5%), weight gain (5%), syncope (5%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Known hypersensitivity reaction to trazodone. Use of a MAOI within 4 weeks of stopping trazodone, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of trazodone within 4 weeks of stopping a MAOI. **Warnings and Precautions:** Clinical worsening and suicide risk, serotonin syndrome, hypomanic/manic switch, QT prolongation, use in patients with heart disease (e.g., recent MI), orthostatic hypotension and syncope, abnormal bleeding, **priapism**, hyponatremia, discontinuation syndrome. **Metabolism/Pharmacogenomics:** 3A4. **Significant drug-drug interactions:** Use caution with potent 3A4 inhibitors (e.g., ketoconazole and protease inhibitors) and enzyme inducers (e.g., carbamazepine and St. John's wort). Check all drug-drug interactions. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk /Not Recommended. **Dosage Form:** Tablet (IR), capsule (ER). **Generic available:** IR: Yes; ER: No. **Cost:** IR **¢**. ER **\$\$**. **FDA label for trazodone from dailymed.nlm.nih.gov, Rev. 2.2009.** **FDA label information from Drugs @FDA for Oleptro dated 11.13.2012.**

VENLAFAXINE (EFFEXOR - IR: IMMEDIATE RELEASE; ER/ XR: SUSTAINED RELEASE)

DOSING INFORMATION: **Effexor XR:** Week 1: Baseline blood pressure, weight. Consider BMP for baseline sodium in older adults. **Start XR:** 75 mg qday (37.5 mg for panic disorder). Week 2: Increase to the **Initial Target Dose (XR)** of 150 mg qday, if tolerated. **OF NOTE**, the initial target dose for social phobia is 75 mg qday and the initial target dose for neuropathic pain is 225 mg qday. Week 4 and Beyond: Consider further increases in 75 mg/day increments every 2 weeks as needed and tolerated. **Typical Dosage Range (XR): 150-300 mg/day. Max Dose (XR):** 300 mg qday. **Effexor IR:** Week 1: Baseline blood pressure, weight. Consider BMP for baseline sodium in older adults. **Start IR:** 37.5 mg bid (37.5 qday with panic disorder). Week 2: Increase to the **Initial Target Dose** of 75 mg bid, if tolerated. **OF NOTE**, the initial target dose for social phobia is 37.5 mg bid qday and the initial target dose for neuropathic pain is 112 mg bid. Week 3 and Beyond: Can consider further increases in 75 mg/day increments every 7 days as needed and tolerated. **Typical Dosage Range (IR): 150-300 mg/day. Max Dose IR:** 375 mg/day. **Discontinuation:** *Often problematic.* 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: Blood pressure, weight. Consider posttreatment BMP to rule out hyponatremia in older adults

GENERAL INFORMATION: Mechanism of Action: Serotonin/Norepinephrine Reuptake Inhibitor (SNRI). **FDA Indications:** GAD, MDD, Panic Disorder, Social Anxiety Disorder. **Off-Label Indications:** Neuropathic pain, other anxiety. **Pharmacokinetics:** T_{1/2} = 5 hrs and 11 hrs (active metabolite). **Common Side effects (MDD, XR):** Nausea (31%), dizziness (20%), somnolence (17%), insomnia (17%), abnormal ejaculation (16%), sweating (14%), dry mouth (12%), nervousness (10%), anorexia (8%), constipation (8%), abnormal dreams (7%), tremor (5%), blurry vision (5%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Known hypersensitivity reaction to the product, use of a MAOI within 14 days of stopping Effexor, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Effexor within 14 days of stopping a MAOI. **Warnings and Precautions:** Clinical worsening and suicide risk, serotonin syndrome, hypomanic/manic switch, sustained hypertension, elevations in systolic and diastolic blood pressure, seizures, mydriasis/ narrow angle glaucoma, discontinuation symptoms, insomnia and nervousness, weight loss and decreased appetite, abnormal bleeding, serum cholesterol elevation, interstitial lung disease and eosinophilic pneumonia.

Metabolism/Pharmacogenomics: Metabolized by 2D6. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Limited drug-drug interactions, Low protein binding, check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk /Not Recommended. **Dosage Forms:** Tablet, Capsule, Coated Tablet (Do not cut, crush or chew). **Generic available:** IR/ER: Yes. **Cost:** IR/ER **¢**. **FDA label information from Drugs @FDA for Effexor XR dated 12.18.2012.**

ANXIOLYTICS & HYPNOTIC MEDICATIONS

ALPRAZOLAM (IR: IMMEDIATE RELEASE; XR: SUSTAINED RELEASE)

DOSING INFORMATION: **Anxiety Disorders:** Consider CBC and LFTs (see **MONITORING**); **Xanax IR:** Week 1: **Start**

IR: 0.25 to 0.5 mg tid; OF NOTE: Scheduled dosing is typically more effective than PRN dosing for control of anxiety symptoms. Week 2 and beyond: Increase dose as needed and tolerated to the minimally effective dose. **Typical Dosage Range IR**: 0.5 to 1 mg tid. **Max Dose IR**: 4 mg/day. **Panic Disorder**: Consider CBC and LFTs (see *MONITORING*); **Xanax IR**: *Week 1: Start IR*: 0.5 mg tid. OF NOTE: Scheduled dosing is typically more effective than PRN dosing for control of anxiety symptoms; Week 2 and beyond: Increase dose as needed and tolerated in 0.5-1 mg/day increments each week to the minimally effective dose. **Typical Dosage Range IR**: 4-6 mg/day. **Max Dose IR**: 9 mg/day. **Xanax XR (Panic Disorder)**: *Week 1: Start XR*: 0.5-1 mg qAM. OF NOTE: Scheduled dosing is typically more effective than PRN dosing for control of anxiety symptoms; Week 2 and beyond: Increase dose as needed and tolerated in 0.5-1 mg/day increments each week to the minimally effective dose to the minimally effective dose. **Typical Dosage Range (XR)**: 3-6 mg/day. **Max Dose XR**: 6 mg/day. **Discontinuation**: Uniquely problematic withdrawal syndrome; Recommended taper of no more than 0.5 mg every 3 days; Doses above 4 mg/day may need slower taper of 10% per month. OF NOTE: Alprazolam concentrations may be reduced by up to 50% in smokers compared to non-smokers.

MONITORING: Consider UTOX if abuse/diversion is a concern. Per FDA: “periodic” blood counts and liver-function tests are recommended for patients on long-term therapy.

GENERAL INFORMATION: Mechanism of action: enhances activity of GABA (benzodiazepine). **FDA Indications**: Panic Disorder; Anxiety disorders; Short-term use for anxiety symptoms. **Other Indications**: Insomnia.

Pharmacokinetics: T_{1/2} = 11 hrs; Onset: Rapid. **Common Side effects (IR—panic disorder)**: Drowsiness (77%), impaired coordination (40%), memory impairment (33%), increased appetite (33%), cognitive disorder (29%), weight gain (27%), constipation (26%), dysarthria (23%), weight loss (23%), decreased libido (14%), micturition difficulties (12%), increased libido (8%), sexual dysfunction (7%). **Black Box Warning**: None. **Contraindications**: Known hypersensitivity reaction to the product. Use in patients with acute narrow angle glaucoma.

Coadministration with ketoconazole or itraconazole. **Warning/Precautions**: Dependence and withdrawal reactions, including seizures, status epilepticus, interdose symptoms, CNS depression and impaired performance, risk of fetal harm, use with CYP 3A inhibitors, hypomanic/manic switch, weak uricosuric effect, respiratory depression, sleep apnea/COPD, physical and psychological dependence, abuse potential, use in the elderly and in patients with liver disease, paradoxical reactions. **Metabolism/Pharmacogenomics**: **Metabolized by CYP3A**.

Significant drug-drug interactions: Use with a great deal of caution with potent 3A inhibitors (e.g., ketoconazole and protease inhibitors) and enzyme inducers (e.g., carbamazepine and St. John’s wort)—see also under contraindications; Use with caution with other sedative/hypnotics. Check all drug-drug interactions. **Pregnancy: Category D; associated w/ increased risk of teratogenesis (need to inform women of childbearing age of this risk)**. **Breastfeeding**: Excreted in breast milk/Not Recommended. **Dosage Form**: Tablet, Oral dissolving tablet, Oral solution, Coated Tablet (Do not cut, crush or chew). **Generic available**: IR/XR: Yes. Cost: IR €, XR \$. **FDA label information from Drugs @FDA for Xanax dated 8.23.2011. FDA label information from Drugs @FDA for Xanax XR dated 8.23.2011.**

BUSPIRONE (BUSPAR)

DOSING INFORMATION: Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start**: 7.5 mg bid. Week 2: Increase to an **Initial Target Dose** of 15 mg bid, if tolerated; Consider further increases as needed and tolerated. **Typical Dose Range**: 15 mg bid to 30 mg bid mg. **Max Dose**: 30 mg bid. OF NOTE: Time frame for improvement similar to SSRIs and other antidepressants. **Discontinuation**: Taper slowly to minimize withdrawal symptoms.

MONITORING: Weight. Consider posttreatment BMP to rule out hyponatremia in older adults. **GENERAL INFORMATION: Mechanism of Action**: Not specifically known; high affinity for serotonin (5-HT_{1A}) receptors and moderate affinity for dopamine (D₂) receptors; Not related to benzodiazepines and does not affect GABA binding. OF NOTE: BuSpar will not mitigate benzodiazepine withdrawal. **FDA Indications**: Anxiety. **Other Indications**: Depression augmentation. OF NOTE: BuSpar may be helpful for reversing SSRI/SNRI induced sexual dysfunction. **Pharmacokinetics**: T_{1/2}: 2-3 hrs. **Common Side effects (Anxiety)**: Dizziness (12%), nausea (8%), headache (6%), nervousness (5%). **Black Box Warning**: None. **Contraindications**: Known hypersensitivity reaction to the product. **Warnings/Precautions**: Use of a MAOI within 14 days of stopping BuSpar, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of BuSpar within 14 days of stopping a MAOI, use in

patients with severe hepatic or renal impairment, potential restlessness syndrome (e.g., akathisia).

Metabolism/Pharmacogenomics: **Metabolized by CYP3A4.** **Significant drug-drug interactions:** Use with a great deal of caution with potent 3A inhibitors (e.g., ketoconazole and protease inhibitors) and enzyme inducers (e.g., carbamazepine and St. John's wort); Avoid grapefruit juice. Check all drug-drug interactions before prescribing. **Pregnancy:** Category B. **Breastfeeding:** No data/Not Recommended. **Dosage Form:** Tablet. **Generic available:** Yes. **Cost:** €. **FDA label information from Drugs @FDA for BuSpar dated 11.22.2010.**

CLONAZEPAM (KLONOPIN)

DOSING INFORMATION: Week 1: Consider CBC and LFTs (see *MONITORING*); **Start:** 0.25 mg bid; OF NOTE: Scheduled dosing is typically more effective than PRN dosing for control of anxiety symptoms. Week 2: Increase dose as needed and tolerated to the **Typical Initial and Target Dosage** of 0.5 mg bid. Can give more of dose at qHS to target insomnia, or if causing excessive daytime sedation. Week 3 and beyond: Can consider further increases as needed and tolerated however most individuals experience less efficacy with more side effects at higher dosing. **Max Dose:** 4 mg/day. **Rapid Discontinuation:** 0.125 mg bid every 3 days. **Extended Discontinuation** (e.g., after months/years of use): 10% per month.

MONITORING: Consider UTOX if abuse/diversion is a concern. Per FDA: "periodic" blood counts and liver-function tests are recommended for patients on long-term therapy.

GENERAL INFORMATION: Mechanism of action: enhances activity of GABA (benzodiazepine). **FDA Indications:** Panic disorder. **Other Indications:** GAD, Social phobia. **Pharmacokinetics:** T_{1/2} 30-40 hrs; Onset: intermediate (1-4 hrs). **Common Side effects (Panic Disorder):** Somnolence (37%), dizziness (8%), upper respiratory tract infection (8%), depression (7%), abnormal coordination (6%), ataxia (5%). **Black Box Warning:** None. **Contraindications:** Known hypersensitivity reaction to the product, patients with clinical or biochemical evidence of significant liver disease, acute narrow angle glaucoma. **Warning/Precautions:** Cognitive/motor impairment, suicidal behavior/ideation, risk of fetal harm, withdrawal symptoms, respiratory depression, sleep apnea/COPD, worsening of seizures, need for periodic blood counts and liver function tests (see above under *MONITORING*) physical and psychological dependence, abuse potential, use in the elderly, increased salivation, caution in renally impaired patients, paradoxical reaction. **Metabolism/Pharmacogenomics:** **Metabolized by CYP3A.** **Significant drug-drug interactions:** Use with a great deal of degree of caution with potent 3A4 inhibitors (e.g., ketoconazole and protease inhibitors) and enzyme inducers (e.g., carbamazepine and St. John's wort); Use caution with other sedative/hypnotics. Check all drug-drug interactions before prescribing. **Pregnancy: Category D; associated w/ increased risk of teratogenesis (need to inform women of childbearing age of this risk).** **Breastfeeding:** Excreted in breast milk/Not Recommended. **Dosage Form:** Tablet, Oral dissolving tablet. **Generic available:** Yes. **Cost:** €. **FDA label information from Drugs @FDA for Klonopin dated 10.31.2013.**

DIAZEPAM (VALIUM)

DOSING INFORMATION: Week 1: Consider CBC and LFTs (see *MONITORING*); **Start:** 5 mg bid. OF NOTE: Scheduled dosing is typically more effective than PRN dosing for control of anxiety symptoms. Week 2: Increase dose as needed and tolerated by 5-10 mg/day increments per week to the minimally effective dose; Can give more of dose at qHS to target insomnia, or if causing excessive daytime sedation. **Typical Dosage Range:** 10-20 mg/day. **Max Dose:** 40 mg/d. **Rapid Discontinuation:** 10% of total dose every 3-4 days. **Extended Discontinuation** (e.g., after months/years of use): 10% per month.

MONITORING: Consider UTOX if abuse/diversion is a concern. Per FDA: "periodic" blood counts and liver-function tests are recommended for patients on long-term therapy.

GENERAL INFORMATION: Mechanism of action: Enhances activity of GABA (benzodiazepine). **FDA Indications:** Anxiety disorder, Acute alcohol withdrawal. **Pharmacokinetics:** T_{1/2} up to 48 hrs, active metabolite: up to 100 hours; Onset: immediate (1-1.5 hrs). **Common Side effects (Anxiety):** Drowsiness, fatigue, muscle weakness, ataxia. **Black Box Warning:** None. **Contraindications:** Known hypersensitivity reaction to the product, myasthenia gravis, severe respiratory insufficiency, severe hepatic insufficiency, sleep apnea syndrome, acute narrow angle glaucoma. **Warning/Precautions:** Cognitive/motor impairment, suicidal behavior/ideation, risk of fetal harm, withdrawal symptoms, respiratory impairment, hepatic insufficiency, worsening of seizures, physical and psychological dependence, abuse potential, use in the elderly, paradoxical reaction, psychotic patients.

Metabolism/Pharmacogenomics: Metabolized by CYP3A4 and 2C19 to active metabolites and largely eliminated by glucuronidation. Use caution in 2C19 poor metabolizers. **Significant drug-drug interactions:** Use with a great deal of caution with potent 3A inhibitors (e.g., ketoconazole and protease inhibitors) and enzyme inducers (e.g., carbamazepine and St. John's wort) as well as with 2C19 inhibitors; Check all drug-drug interactions before prescribing. **Pregnancy: Category D; associated w/ increased risk of teratogenesis (need to inform women of childbearing age of this risk).** **Breastfeeding:** Excreted in breast milk/Not Recommended. **Significant drug-drug interactions:** Check all drug-drug interactions. Use with caution with other sedative/hypnotics. **Dosage Form:** Tablet, Oral solution. **Generic available:** Yes. **Cost:** €. **FDA label information from Drugs @FDA for Valium dated 10.22.2013.**

ESZOPICLONE (LUNESTA)

DOSING INFORMATION: Week 1: **Start:** 2 mg qHS (1 mg qHS in patients who are elderly, hepatically impaired or taking a 3A4 inhibitor). Week 2: Consider an increase in dose to 3 mg qHS for more effective sleep maintenance (2 mg qHS in patients who are elderly, hepatically impaired, or taking a 3A4 inhibitor), if tolerated. **Typical Dosage Range:** 2-3 mg qHS (1-2 mg qHS in patients who are elderly, hepatically impaired, or taking a 3A4 inhibitor). **Max Dose:** 3 mg qHS (2 mg qHS in patients who are elderly, hepatically impaired, or taking a 3A4 inhibitor). **OF NOTE:** Do not take immediately after a meal—much less effective. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

MONITORING: None indicated.

GENERAL INFORMATION: Mechanism of action: Non-benzodiazepines hypnotic that acts at the GABA receptor complex. **FDA Indications:** Treatment of insomnia. **Pharmacokinetics:** T_{1/2} = 6 hrs. **Common Side effects (2 mg, Insomnia):** headache (21%), unpleasant taste (17%), somnolence (10%); dry mouth (5%). **Black Box Warning:** None. **Contraindications:** Known hypersensitivity reaction to the product. **Warnings/Precautions:** Need to evaluate for co-morbid diagnoses, severe anaphylactic/anaphylactoid reaction, abnormal thinking, behavioral changes and complex behaviors (e.g., "sleep driving", "sleep eating" and hallucinations), withdrawal effects (monitor for tolerance, abuse, and dependence), cognitive/motor impairment, use in the elderly, use in patients with hepatic impairment, impaired respiratory function, impaired drug metabolism or hemodynamic responses. **Metabolism/Pharmacogenomics:** Metabolized by 3A4 and 2E1. **Significant drug-drug interactions:** Use with caution with potent 3A4 inhibitors (e.g., ketoconazole and protease inhibitors) and enzyme inducers (e.g., carbamazepine and St. John's wort); Use with caution with other sedative/hypnotics. Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** No data/Not recommended. **Dosage Form:** Tablet. **Generic available:** Yes. **Cost:** \$\$\$. **FDA label information from Drugs @FDA for Lunesta dated 2.3.2014.**

HYDROXYZINE PAMOATE (VISTARIL), HYDROXYZINE HYDROCHLORIDE (ATARAX)

DOSING INFORMATION: Week 1: **Start:** 25 mg q6 hrs. Week 2: Increase if needed and tolerated to the **Initial Target Dose** of 50 mg q 6 hrs. Week 3: Can consider further increases in dose in 25 mg q6 hr increments, if needed and tolerated. **OF NOTE:** Can start at 50 mg q6 hrs and titrate up to 100 mg q 6hr more quickly, if needed. **Typical Dosage Range:** 50-100 mg q6hrs. **Max Dose:** 400 mg/day. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

MONITORING: None indicated.

GENERAL INFORMATION: Mechanism of action: Antihistamine (H₁-receptor). **FDA Indications:** Anxiety. **Non-FDA Indications:** Insomnia. **Pharmacokinetics:** T_{1/2} 20-25 hrs. Onset within 15 to 30 minutes. **Common Side effects (Anxiety):** Drowsiness; dry mouth. **Black Box Warning:** None. **Contraindications:** Use in early pregnancy. Known hypersensitivity reaction to the product. **Warning/Precautions:** Use with other CNS depressants, cognitive/motor impairment, use in elderly patients. **Metabolism/Pharmacogenomics:** Metabolized in the liver. Specific pathways are unknown. **Significant drug-drug interactions:** Check all drug-drug interactions before prescribing. **Pregnancy:** Category C (except 1st trimester). **Breastfeeding:** Excreted in breast milk/Not Recommended. **Significant drug-drug interactions:** Use with caution with sedatives/hypnotics. Check all drug-drug interactions before prescribing. **Dosage Form:** Generic available: Yes. **Cost:** €. **FDA label for Atarax from dailymed.nlm.nih.gov, Rev. 6.2006. FDA label for Vistaril from dailymed.nlm.nih.gov, Rev. 6.2006.**

LORAZEPAM (ATIVAN)

DOSING INFORMATION: Week 1: Consider CBC and LFTs (see *MONITORING*); **Start:** 0.5 mg bid; OF NOTE: Scheduled dosing is typically more effective than PRN dosing for control of anxiety symptoms. Week 2: Increase dose as needed and tolerated to the **Initial Target Dose** of 1 mg bid. Can give more of the dose at qHS to target insomnia or if causing excessive daytime sedation. Week 3 and beyond: Consider further increases as needed and tolerated to the minimally effective dose. **Typical Target Dose:** 1-3 mg bid. **Max Dose:** 10 mg/day. **Rapid discontinuation:** 10% every 3 days. **Extended Discontinuation** (e.g., after months/years of use): 10% per month. **MONITORING:** Consider UTOX if abuse/diversion is a concern. Per FDA: “periodic” blood counts and liver-function tests are recommended for patients on long-term therapy.

GENERAL INFORMATION: Mechanism of action: enhances activity of GABA (benzodiazepine). **FDA Indications:** Anxiety disorders; Short-term use for anxiety symptoms or anxiety associated with depressive symptoms. **Other Indications:** Insomnia (1-4 mg qHS). **Pharmacokinetics:** $T_{1/2}$ = 12 hrs; Onset: intermediate (2 hrs); OF NOTE: no active metabolites, so safer in liver disease. **Common Side effects (Anxiety):** Sedation (15.9%), dizziness (6.9%), weakness (4.2%), unsteadiness (3.4%). **Black Box Warning:** None. **Contraindications:** Known hypersensitivity reaction to the product. Acute narrow-angle glaucoma. **Warning/Precautions:** Cognitive/motor impairment, suicidal behavior/ideation, worsening of depression, risk of fetal harm, withdrawal symptoms, respiratory depression, caution in patients with sleep apnea/COPD, with hepatic insufficiency and/or encephalopathy, and in the elderly, physical and psychological dependence, abuse potential, paradoxical reaction.

Metabolism/Pharmacogenomics: Largely eliminated by glucuronidation. **Significant drug-drug interactions:** Use with caution with other sedative/hypnotics. Check all drug-drug interactions. **Pregnancy: Category D; associated w/ increased risk of teratogenesis (need to inform women of childbearing age of this risk).** **Breastfeeding:** Excreted in breast milk/Not Recommended. **Dosage Form:** Oral solution, Tablet, IV. **Generic available:** Yes. **Cost:** ¢. **FDA label information from Drugs @FDA for Ativan dated 4.18.2007.**

TEMAZEPAM (RESTORIL)

DOSING INFORMATION: Week 1: **Start:** 15 mg qHS, the **Initial Target Dose** (7.5 mg qHS in the elderly). Week 2: Assess for side effects, can increase as needed to 30 mg qHS (15 mg qHS in the elderly), if tolerated. **Typical Dosage Range:** 15-30 mg qHS (7.5-15 mg qHS in the elderly). OF NOTE: Some adult patients find the 7.5 mg qHS sufficient to improve sleep latency. **Max Dose:** 30 mg qHS (15 mg qHS in the elderly). **Discontinuation:** No taper needed, if less than 10 days use; Recommend taper 10% every 3 days (or longer) with long-term use.

MONITORING: Consider UTOX if abuse/diversion is a concern. Per FDA: “periodic” blood counts and liver-function tests are recommended for patients on long-term therapy.

GENERAL INFORMATION: Mechanism of action: enhances activity of GABA (benzodiazepine hypnotic). **FDA Indications:** Short-term use for insomnia (7-10 days). **Pharmacokinetics:** $T_{1/2}$ = 8.8 hrs; Onset: rapid (0.5 hr). **Common Side effects (Insomnia):** Drowsiness (9%). **Black Box Warning:** None. **Contraindications:** Known hypersensitivity reaction to the product. **Women who are or may become pregnant.** **Warnings/Precautions:** Need to evaluate for co-morbid diagnoses, severe anaphylactic/anaphylactoid reaction, abnormal thinking, behavioral changes and complex behaviors (e.g., “sleep driving”, “sleep eating” and hallucinations), withdrawal effects, cognitive/motor impairment, use in the elderly, use in patients with hepatic impairment, impaired drug metabolism or hemodynamic responses, disinhibition, suicidal behavior/ideation, worsening of depression, physical and psychological dependence, withdrawal syndrome, abuse potential. **Metabolism/Pharmacogenomics:** Metabolized via conjugation. **Significant drug-drug interactions:** Use with caution with other sedative/hypnotics. Check all drug-drug interactions before prescribing. **Pregnancy: Category X/Established risk of congenital malformations (need to inform women of childbearing age of this risk).** **Breastfeeding:** Excreted in breast milk/Not Recommended. **Dosage Form:** Capsule. **Generic available:** Yes. **Cost:** ¢. **FDA label information from Drugs @FDA for Restoril dated 11.8.2010.**

ZALEPLON (SONATA)

DOSING INFORMATION: Week 1: **Start:** 10 mg qHS the **Initial Target and Typical Dose** (5 mg qHS for elderly, debilitated, or hepatically impaired patients) **Max Dose:** 20 mg qHS (10 mg qHS for elderly, debilitated, hepatically

impaired patients). **OF NOTE:** Very short acting. Should not be taken with or immediately after a meal due to decreased efficacy. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

MONITORING: None indicated.

GENERAL INFORMATION: Mechanism of action: Non-benzodiazepine hypnotic that acts at the benzodiazepine receptor (GABA-A). **FDA Indications:** Short-term treatment of insomnia. **Pharmacokinetics:** $T_{1/2} = 1$ hr. **Common Side effects (Insomnia):** Abdominal pain (6%). **Black Box Warning:** None. **Contraindications:** Known hypersensitivity reaction to the product. **Warnings/Precautions:** Need to evaluate for co-morbid diagnoses, abnormal thinking, behavioral changes and complex behaviors (e.g., “sleep driving”, “sleep eating” and hallucinations), severe anaphylactic/anaphylactoid reaction, worsening of depression or suicidal thinking, withdrawal effects (monitor for tolerance, abuse, and dependence), CNS depressant effects with cognitive/motor impairment, use in the elderly, use in patients with hepatic impairment, impaired respiratory function, impaired drug metabolism or hemodynamic responses. **Metabolism/Pharmacogenomics:** Metabolized by aldehyde oxidase and to a lesser extent by 3A4. **Significant drug-drug interactions:** Use with caution with other sedative/hypnotics. Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk/ Not Recommended. **Dosage Form:** Capsule. **Generic available:** Yes. Cost: €. **FDA label information from Drugs @FDA for Sonata dated 4.19.2013.**

ZOLPIDEM (AMBIEN, AMBIEN CR, INTERMEZZO)

DOSING INFORMATION: Ambien (Ambien CR): Week 1: **Men Start:** 5-10 mg qHS (**CR:** 6.25-12.5 mg qHS); **Women Start:** Ambien 5 mg qHS (**CR:** 6.25 mg); **Elderly, debilitated, or hepatically impaired Start:** 5 mg (B: 6.25 mg qHS). Week 2: Assess for side effects. **Typical Target Dose:** 5-10 mg qHS (Ambien CR 6.25-12.5 mg qHS). **Max Dose:** 10 mg qHS (**CR:** 12.5mg qHS). **OF NOTE:** Short acting. Should not be taken with or immediately after a meal due to decreased efficacy.

MONITORING: None indicated.

GENERAL INFORMATION: Mechanism of action: Non-benzodiazepines hypnotic that acts at the benzodiazepine receptor (GABA-A Agonist). **FDA Indications:** Short-term treatment of insomnia. **Pharmacokinetics:** $T_{1/2} = 2.6$ hrs. **Common Side effects (Insomnia):** Drowsiness (8%), dizziness (5%). **Black Box Warning:** None. **Contraindications:** Known hypersensitivity reaction to the product. **Warnings/Precautions:** CNS depressant effects with cognitive/motor impairment including next day impairment, need to evaluate for co-morbid diagnoses, severe anaphylactic/anaphylactoid reaction, abnormal thinking, behavioral changes and complex behaviors (e.g., “sleep driving”, “ sleep eating” and hallucinations), worsening of depression or suicidal thinking, withdrawal effects (monitor for tolerance, abuse, and dependence), respiratory depression. **Metabolism/Pharmacogenomics:** Metabolized by multiple P450 enzymes. **Significant drug-drug interactions:** Use with caution with other sedative/hypnotics. Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk/Use Caution. **Dosage Form:** Oral solution, Tablet, Sublingual. **Generic available:** Yes. Cost: €. **FDA label information from Drugs @FDA for Ambien dated 4.19.2013.**

ADHD MEDICATIONS

ATOMOXETINE (STRATTERA)

DOSING INFORMATION: Week 1: Evaluate cardiovascular risk (e.g., presence of structural cardiac abnormalities or other serious heart problems) and screen for psychosis and bipolar disorder; Baseline HR, BP and consider EKG; **Start:** 40 mg qAM. Week 2: Increase to 80 mg qAM (or 40 mg bid, the **Initial Target and Typical Dose**), if tolerated. Week 4-6: Assess for side effects; can consider further increase to 100 mg/day if still symptomatic. **Max Dose:** 100 mg qAM. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

MONITORING: BP and HR at baseline, 1 month, then every 6 to 12 months; hepatic function tests if signs of liver dysfunction.

GENERAL INFORMATION: Mechanism of action: Selective norepinephrine reuptake inhibitor. **FDA Indication:** ADHD. **Pharmacokinetics:** $T_{1/2} = 5.2$ hrs. **Common Side effects (ADHD):** nausea (26%), dry mouth (20%), decreased appetite (16%), insomnia (15%), fatigue (10%), constipation (8%), dizziness (8%), somnolence (8%), erectile dysfunction (8%), abdominal pain (7%), urinary hesitation, (6%) and irritability (5%). **Black Box Warning:** Increased

risk of suicidal ideation in children or adolescents, monitor closely. **Contraindications:** Known hypersensitivity reaction to the product. Use of a MAOI within 14 days of stopping Strattera, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Strattera within 14 days of stopping a MAOI, narrow angle glaucoma, pheochromocytoma, severe cardiovascular disorders. **Warnings/Precautions:** Suicidal ideation, severe liver injury, serious cardiovascular events, emergent cardiovascular symptoms, effects on blood pressure and heart rate including hypertension, tachycardia, orthostasis and syncope, emergent psychotic or manic symptoms—screening for bipolar disorder is recommended, aggressive behavior/hostility, possible severe allergic reactions including anaphylaxis, urinary hesitancy and retention, **priapism**, use in patients receiving potent 2D6 inhibitors (e.g., fluoxetine or paroxetine) or who are known to be 2D6 poor metabolizers as dosage adjustments may be necessary. **Metabolism/Pharmacogenomics:** Metabolized by 2D6. Use with great caution and consider alternatives to Strattera in 2D6 poor metabolizers. **Significant drug-drug interactions:** Use with great caution and consider alternatives to Strattera when considering use with 2D6 inhibitors (e.g., fluoxetine or paroxetine); Check all drug-drug interactions and **CONSIDER CONSULTATION WITH A PHARMACIST BEFORE PRESCRIBING THIS MEDICATION.** **Pregnancy:** Category C. **Breastfeeding:** Limited data/Not recommended. **Dosage Form:** Capsule. **Generic available:** No. **Cost:** \$\$\$ **FDA label information from Drugs @FDA for Strattera dated 2.20.14.**

D-AMPHETAMINE AND L-AMPHETAMINE SALTS (ADDERALL IR: IMMEDIATE RELEASE; XR: SUSTAINED RELEASE)

DOSING INFORMATION: **Adderall IR:** Week 1: Evaluate cardiovascular risk (e.g., presence of structural cardiac abnormalities or other serious heart problems); Baseline HR, BP and consider EKG; Screen for bipolar disorder; **Start IR:** 5 mg qAM and 5 mg qPM (use intervals of 4-6 hours between doses—can take earlier in the afternoon if insomnia results). Week 2: Increase to 10 mg qAM and 5 mg qPM, if needed and tolerated. Week 3 and beyond: Consider further increases in 5 mg qday per week increments, if tolerated, until treatment of symptoms or max dose is reached. **Adderall XR:** Week 1: Evaluate cardiovascular risk (e.g., presence of structural cardiac abnormalities or other serious heart problems); Baseline HR, BP and consider EKG; Screen for bipolar disorder. **Start XR:** 10 mg qAM. Week 2: Consider increase to 20 mg qAM, if needed and tolerated. Week 3 and beyond: Consider further increases in 10 mg qAM increments per week, if tolerated, until treatment of symptoms, or max dose is reached. **Typical Target Dose (IR/XR):** Lowest effective individualized dose. **Usual Max Dose (IR/XR):** 40 mg/day.

MONITORING: BP and HR at baseline, 1 month, then every 6 to 12 months; Signs of aggressive behavior or hostility; Consider UTOX if abuse/diversion is a concern.

GENERAL INFORMATION: **Mechanism of action:** CNS stimulant. **FDA Indication:** **IR:** ADHD in children, narcolepsy. **XR:** ADHD in children and adults. **Pharmacokinetics:** T_{1/2} = 10-13 hrs. **Common Side effects (ADHD, XR):** Dry mouth (35%), loss of appetite (33%), insomnia (27%), headache (26%), weight loss (10%), nausea (8%), anxiety, (8%), dizziness (7%), tachycardia (6%), diarrhea (6%), urinary tract infections (5%). **Black Box Warnings:** High potential for abuse/dependence; Misuse may cause sudden death and serious cardiovascular adverse events.

Contraindications: Known hypersensitivity reaction to the product. Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma, agitated states, history of drug abuse, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Adderall within 14 days of stopping a MAOI. **Warnings/Precautions:** Serious cardiovascular events (death, stroke, and myocardial infarction)—**stimulant drugs should not be used in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious heart problems**, increased blood pressure, adverse psychiatric events (may worsen pre-existing psychosis or bipolar disorder or trigger the emergence of new psychotic or manic symptoms—screening for bipolar disorder is recommended), monitor for aggressive behavior, seizures, peripheral vasculopathy including Raynaud's phenomenon, visual disturbance, may worsen tics, potential for abuse of dependence. **Metabolism/Pharmacogenomics:** Metabolized by 2D6. **Significant drug-drug interactions:** Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** No data/Not recommended. **Dosage Form:** Tablet (IR), Capsule (XR). **Generic available:** IR/XR: Yes. **Cost:** \$. **FDA label information from Drugs @FDA for Adderall XR dated 2.7.2007.** **FDA label information from Drugs @FDA for Adderall XR dated 12.3.2013.**

LISDEXAMFETAMINE (VYVANSE)

DOSING INFORMATION: Week 1: Evaluate cardiovascular risk (e.g., presence of structural cardiac abnormalities or other serious heart problems); Baseline HR, BP and consider EKG; **Start:** 30 mg qAM. Week 2: Increase dose in weekly increments of 10 mg-20 mg, if tolerated, until treatment of symptoms or max dose is reached. **Typical Target Dose:** Lowest effective individualized dose. **Usual max dose:** 70 mg/day.

MONITORING: BP and HR at baseline, 1 month, then every 6 to 12 months; Signs of aggressive behavior or hostility; Consider UTOX if abuse/diversion is a concern.

GENERAL INFORMATION: Mechanism of action: CNS stimulant. **FDA Indication:** ADHD in children and adults.

Pharmacokinetics: $T_{1/2}$ = < 1 hour (pro-drug for dextroamphetamine $T_{1/2}$ = 10 hrs). **Common Side effects (ADHD):** Decreased appetite (27%), insomnia (27%), dry mouth (26%), diarrhea (7%), nausea (7%), anxiety (6%) and anorexia (5%). **Black Box Warnings:** CNS stimulants have a high potential for abuse/dependence; Assess for risk of abuse prior to and after prescribing. **Contraindications:** Known hypersensitivity reaction to the product. Concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Vyvanse within 14 days of stopping a MAOI. **Warnings/Precautions:** Serious cardiovascular events (death, stroke, and myocardial infarction)—**stimulant drugs should not be used in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious heart problems,** blood pressure and heart rate increases, adverse psychiatric events (may worsen pre-existing psychosis or bipolar disorder or trigger the emergence of new psychotic or manic symptoms—screening for bipolar disorder is recommended), monitor for aggressive behavior, peripheral vasculopathy including Raynaud's phenomenon, potential for abuse of dependence. **Metabolism/Pharmacogenomics:** Converted to dextroamphetamine in the blood. Dextroamphetamine metabolized by 2D6. **Significant drug-drug interactions:** Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** No data/Not recommended. **Dosage Form:** Capsule. **Generic available:** No. **Cost:** \$\$\$. **FDA label information from Drugs @FDA for Vyvanse dated 12.6.13.**

METHYLPHENIDATE (IMMEDIATE RELEASE (IR): RITALIN, METHYLPHENIDATE SUSTAINED RELEASE (SR): METADATE ER, METHYLIN ER, RITALIN SR; METADATE CD, RITALIN LA, CONCERTA, DAYTRANA-PATCH, QUILLIVANT XR)

DOSING INFORMATION: Ritalin IR: Week 1: Evaluate cardiovascular risk (e.g., presence of structural cardiac abnormalities or other serious heart problems); Baseline HR, BP and consider EKG; **Start IR:** 5 mg qAM and 5 mg qPM (preferably before meals; use intervals of 4-6 hours between doses; can take earlier in the afternoon if insomnia results). Week 2: Increase dose to 10 mg qAM and 5 mg qPM, if needed and tolerated. Week 3 and beyond: Consider further increase in dose in 5 mg/day per week increments, if tolerated, until treatment of or max dosage is reached. **Ritalin SR:** Week 1: Evaluate cardiovascular risk (e.g., presence of structural cardiac abnormalities or other serious heart problems); Baseline HR, BP and consider EKG; **Start SR:** 10 mg qAM (preferably before meals). Week 2: Consider increase to 20 mg qAM, if needed and tolerated. Week 3 and beyond: Consider further increase in dose in 10 mg increments qday per week, if tolerated until treatment of symptoms or max dose is reached. **Concerta:** Week 1: Evaluate cardiovascular risk (e.g., presence of structural cardiac abnormalities or other serious heart problems); Baseline HR, BP and consider EKG; **Start Concerta:** 18 mg qAM. Week 2: Increase dose to 36 mg qAM if needed and tolerated; Week 3 and beyond: Consider further increases in 18 mg qday per week increments, if tolerated, until treatment of symptoms or max dose is reached. **Daytrana:** Patch; Special dosing (see FDA guidelines). **Typical Target Dose (IR/SR/Concerta):** Lowest effective individualized dose. **Usual Max Dose (IR/SR):** 60 mg/day (**Concerta** 72 mg/day).

MONITORING: BP and HR at baseline, 1 month, then every 6 to 12 months; Signs of aggressive behavior or hostility; Consider UTOX if abuse/diversion is a concern. Per FDA: "Periodic CBC, differential, and platelet counts are advised during prolonged therapy."

GENERAL INFORMATION: Mechanism of action: CNS stimulant. **FDA Indication:** ADHD; Narcolepsy.

Pharmacokinetics: $T_{1/2}$ for Concerta: 3.5 hrs (others vary). **Common side effects (ADHD, Concerta):** Decreased appetite (25%), headache (22%), dry mouth (14%), nausea (13%), insomnia (12%), anxiety (8%), weight decreased (7%), irritability (6%), and hyperhidrosis (5%), tachycardia (5%). **Black Box Warnings:** Caution in use in patients with history of drug or alcohol dependence. Chronic abusive use can lead to tolerance and psychological dependence including abnormal behavior. **Contraindications:** Known hypersensitivity reaction to the product,

marked anxiety, tension, and agitation, glaucoma, tics or a family history or diagnosis of Tourette's syndrome, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of methylphenidate within 14 days of stopping a MAOI. **Warnings/Precautions:** Serious cardiovascular events (death, stroke, and myocardial infarction)—**stimulant drugs should not be used in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious heart problems**, blood pressure and heart rate increases, adverse psychiatric events (may worsen pre-existing psychosis or bipolar disorder or trigger the emergence of new psychotic or manic symptoms—screening for bipolar disorder is recommended), monitor for aggressive behavior, seizures, **priapism**, visual disturbance, tics, peripheral vasculopathy including Raynaud's syndrome, GI obstruction with preexisting GI narrowing, hematologic monitoring advised (see above under MONITORING). **Metabolism/Pharmacogenomics:** Primarily metabolized by de-esterification. **Significant drug-drug interactions:** May inhibit the metabolism of Coumadin, anticonvulsants and some antidepressants, e.g., TCAs and SSRIs. Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** No data/Not recommended. **Significant drug-drug interactions:** **Dosage Form:** Tablet, Capsule Extended Release, Patch, Solution, Suspension, Tablet Chewable. **Generic available:** IR/ER. **Cost:** IR \$, ER \$\$ **FDA label information from Drugs @FDA for Concerta dated 12.12.13.**

MISCELLANEOUS MEDICATIONS

NALTREXONE (REVIA, DEPADE)

DOSING INFORMATION: Week 1: Obtain BMP and LFT's as screening labs prior to initiation of naltrexone to assess for renal/hepatic function and rule out acute hepatitis. **Start:** 25 mg qday. Week 2: Increase to an **Initial Target Dose** of 50 mg qday, if tolerated. Week 4 and beyond: The dosage can then be increased in 4-6 weeks, as needed and tolerated, to 75 mg qday. Typical Dosage Range: 50-100 mg/day. **Max Dose:** 100 mg/day. OF NOTE: at least one large randomized controlled study (the COMBINE study) used 100 mg qday, which may be more effective. Naltrexone is not toxic to the liver at lower doses, however, it can become toxic if administered in larger quantities (300 mg qday) or taken in overdose.

MONITORING: Obtain BMP and LFT's as screening labs prior to initiation of naltrexone to assess for renal/hepatic function and rule out acute hepatitis. If screening LFT's are normal, LFT's should be monitored every 1-3 months or sooner if clinically indicated. If screening LFT's are abnormal, rule out acute hepatitis or liver disease and consider monitoring LFT's q 1 month or sooner until they return to normal.

GENERAL INFORMATION: **Mechanism of action:** opiate antagonist. **FDA indications:** Opiate and alcohol dependence. **Off-label indication:** self-injurious behavior. OF NOTE: **Naltrexone will cause opioid withdrawal; thus, it should not be used until the patient is opioid free for 7 to 10 days.** Self-reporting of abstinence from opioids in opioid addicts should be verified by analysis of the patient's urine for absence of opioids. Patients treated with naltrexone should carry a card, for emergency medical care, in case they require treatment with an opioid analgesic. If there is any question of occult opioid dependence, perform a naloxone challenge test and do not initiate naltrexone therapy until the challenge test is negative. **Pharmacokinetics:** T_{1/2} = 4 hrs (naltrexone), 13 hrs (active metabolite). **Common Side effects (Alcohol Dependence):** nausea (10%), headache (7%). **Black Box Warning:** Naltrexone can cause hepatocellular injury when given in excessive doses and is contraindicated in acute hepatitis or liver failure. Use of naltrexone should be discontinued in the event of symptoms or signs of acute hepatitis. **Contraindications:** Known hypersensitivity reaction to the product. Patients receiving opioid analgesics, in opioid withdrawal, or dependent on opioids. Patients with acute hepatitis or liver failure. Any individual who has failed the naloxone challenge test or has a positive urine screen for opioids. **Warnings and Precautions:** Vulnerability to opioid overdose, precipitated opioid withdrawal, hepatotoxicity, depression and suicidality. Eosinophilic pneumonia, hypersensitivity reactions including anaphylaxis. **Patient education:** Patients should be warned of the risk of hepatic injury and advised to stop the use of naltrexone and seek medical attention if they experience symptoms of acute hepatitis. **Metabolism/Pharmacogenomics:** Naltrexone is not metabolized by the P450 system; rather it is metabolized by the cytosolic enzyme dihydrodiol dehydrogenase. **Significant drug-drug interactions:** Check all drug-drug interactions before prescribing. **Pregnancy:** C. **Breastfeeding:** Excreted in breast milk/Use Caution. **Dosage Form:** Tablet (IM available – see FDA <http://www.accessdata.fda.gov/>). **Generic Available:** Yes. **Cost:** \$. **FDA label information from Drugs @FDA for Revia dated 10.3.13.**

PRAZOSIN (MINIPRESS)

DOSING INFORMATION: Week 1: **Start:** 1 mg qHS increase to 2 mg qHS after 3-4 days. Week 2: Continue titration in 1 mg qHS increments every 3-4 days, if tolerated, until symptom remission, or max dose reached. **Typical Dosage Range:** 3-5 mg qHS. **Max Dose:** 10 mg qHS (in severe PTSD).

MONITORING: Blood pressure.

GENERAL INFORMATION: **Mechanism of action:** Antihypertensive (alpha-1 blocker). **Non-FDA Indication:** PTSD-related nightmares/night sweats. **Pharmacokinetics:** $T_{1/2}$ = 2-3 hrs. **Common Side effects (Hypertension):** Dizziness (10%), headache (8%), drowsiness (8%), lack of energy (7%), weakness (6%), palpitations (5%), nausea (5%).

Black Box Warnings: None listed. **Contraindications:** Known hypersensitivity reaction to the product or quinazolines.

Warnings/Precautions: Syncope with loss of consciousness (occasionally associated with severe tachycardia), orthostatic hypotension, cataract surgery, dizziness or drowsiness may occur after first dose.

Metabolism/Pharmacogenomics: Metabolized primarily by demethylation and conjugation. **Significant drug-drug interactions:** Taking with trazodone or Viagra may increase risk **priapism**. Check all drug-drug interactions.

Pregnancy: Category C. **Breastfeeding:** No data/Not recommended. Check all drug-drug interactions before prescribing. **Dosage Form:** Capsules. **Generic available:** Yes. **Cost:** **¢**. **FDA label information from Drugs @FDA for Minipress dated 11.4.13.**

MOOD STABILIZERS

CARBAMAZEPINE EXTENDED RELEASE (TEGRETOL XR; EQUETRO)

DOSING INFORMATION: Week 1: Check baseline labs (urine pregnancy test, CBC with differential, CMP—see below for guidelines regarding Asian patients). Discuss birth control method with women of childbearing age due to severe risk to fetus. **Avoid in pregnancy.** **Start:** 200 mg bid. Week 2-8: Check trough carbamazepine plasma level before the morning dose. If level is sub-therapeutic, increase dosage by 200 mg/day, if tolerated. This process is repeated weekly over 8 weeks due to autoinduction of metabolism. **Target Plasma Level:** Therapeutic levels: 4-12 mcg/ml (**Typical Dosage Range:** 600-1200 mg/day; **Max Dose:** 1600 mg/day). **Toxic concentration:** >15 mcg/ml. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

ONGOING MONITORING: Baseline labs: urine pregnancy test, CBC with differential, CMP. Monitoring of blood levels is recommended with the usual adult therapeutic drug levels between 4 and 12 mcg/ml. This medication induces autoinduction of metabolism, which is usually complete 3-5 weeks after initiation of a fixed carbamazepine regimen. Monitoring frequency (blood level & CBC with differential): Qweekly X 8 weeks, Q2 months X 2, and then q6 months. LFTs: q6 months.

GENERAL INFORMATION: **Mechanism of action:** Antiepileptic drug with mood stabilizer efficacy chemically related to tricyclic antidepressants. **FDA Indications:** Bipolar I, acute manic and mixed episodes.

Pharmacokinetics: $T_{1/2}$ variable due to autoinduction; Initial: 35-40 hours Steady state: 12-17 hours. **Common Side effects (Equetro, Mania):** Dizziness (44%), somnolence (32%), nausea (29%), vomiting (18%), ataxia (15%), constipation (10%), pruritis (8%), dry mouth (8%), asthenia (8%), rash (7%), blurred vision (6%), speech disorder (6%).

Black Box Warnings: (1) Serious and sometimes fatal dermatologic reactions, including toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS). Estimated occurrence: 1 to 6 per 10,000 new users in countries w/ mainly Caucasian populations, but the risk in some Asian countries is estimated 10X higher and are associated with the presence of HLA-B*1502. Asian patients and other high-risk patients should be screened for the presence of HLA-B*1502 prior to starting Equetro. Discontinue, if these reactions occur. (2) Aplastic anemia and agranulocytosis. Obtain pretreatment hematological testing (SEE ABOVE). Discontinue if significant bone marrow depression develops. **Contraindications:** Hypersensitivity to carbamazepine, tricyclic antidepressants, or any component of the formulation; bone marrow depression; concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Equetro within 14 days of stopping a MAOI; concomitant use with nefazodone; concomitant use with delavirdine or other non-nucleoside reverse transcriptase inhibitors. **Warnings and Precautions:** Serious dermatologic reactions (SJS/TEN associated with HLA-B*1502 allele—as noted above, and hypersensitivity reactions associated with HLA-A*3101 allele—consider testing prior to treatment to reduce risk), aplastic anemia and agranulocytosis, drug reaction with eosinophilia and systemic symptoms, suicidal

behavior and ideation, embryofetal toxicity, abrupt discontinuation and risk of seizure, hyponatremia, cognitive and motor impairment, hepatic porphyria, decreased antiviral effect of non-nucleoside reverse transcriptase inhibitors. **Metabolism/Pharmacogenomics:** **Metabolized by 3A4.** **Significant drug-drug interactions:** Equetro is a strong 3A4 inducer and is inhibited by many drugs include fluoxetine. Examples of interactions include with Warfarin (resulting in decreased Warfarin levels) and hormone contraceptives (resulting in reduced efficacy). Check all drug-drug interactions as they are common with this medication and **CONSIDER CONSULTATION WITH A PHARMACIST BEFORE PRESCRIBING THIS MEDICATION.** **Pregnancy: Category D; associated w/ increased risk of teratogenesis (need to inform women of childbearing age of this risk) and should be avoided in pregnancy.** **Breastfeeding:** Excreted in breast milk/Not recommended. Would recommend checking blood levels in the infant/toddler to confirm minimal maternal transfer of this medication given the variability in excretion between mothers. **Dosage Form:** Capsule, Tablet. **Generic Available:** Yes; Equetro: No. **Cost:** Carbamazepine XR \$. **FDA label information from Drugs @FDA for Equetro dated 11.13.12.**

DIVALPROEX SODIUM (ER, STAVZOR (IR))

DOSING INFORMATION: **Depakote ER:** Week 1: Check baseline labs (urine pregnancy test, CBC for thrombocytopenia, coagulation tests, and liver function tests). Discuss birth control method with women of childbearing age due to severe risk to fetus. **Avoid in pregnancy.** **Start ER:** (extended-release) 500 mg qHS. Week 2: Check trough Depakote ER plasma level before, but as close to the dosing time as possible. If level is subtherapeutic, add 250-500 mg to qHS dose, if tolerated. Repeat weekly as need to reach therapeutic dosage. **Target plasma level (ER):** 85 to 125 mcg/ml. **Usual Max Dose:** 60 mg/kg/day. **Formulation:** **Depakote DR** is a less preferable formulation due to increased side effect profile. If used, Depakote DR typically requires lower doses divided bid or TID and a trough plasma level of 50 to 125 mcg/ml. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

ONGOING MONITORING: Weight, CBC, coagulation tests, and liver function tests are recommended before initiating therapy and at least q6 months.

GENERAL INFORMATION: **Mechanism of action:** Antiepileptic drug with mood stabilizer efficacy. **FDA Indications:** Bipolar I disorder, mania or mixed. **Off-Label Indications:** Bipolar I disorder, rapid cycling. **Pharmacokinetics:** $T_{1/2}$ = 9-16 hrs. **Common side effects:** Somnolence (26%), dyspepsia (23%), nausea (19%), vomiting (13%), diarrhea (12%), dizziness (12%), abdominal pain (10%). **Black Box Warnings:** (1) Hepatotoxicity (usually during the first 6 months), (2) pancreatitis and (3) fetal risk particularly including neural tube defects, other major malformations, and decreased IQ. **Contraindications:** Known hypersensitivity reaction to the product. Hepatic disease or significant hepatic dysfunction, known mitochondrial disorders caused by mutations to DNA polymerase gamma, urea cycle disorders, pregnant patients treated for prophylaxis of migraine headaches. **Warnings and Precautions:** Hepatotoxicity, patients with known or suspected mitochondrial disease, birth defects, decreased IQ following in utero exposure, use in women of child bearing potential, pancreatitis, suicidal behavior or ideation, urea cycle disorders, thrombocytopenia, hyperammonemia, hyperammonemia and encephalopathy associated with concomitant topiramate use, hypothermia, multi-organ hypersensitivity reactions, interaction with carbapenem antibiotics, somnolence in the elderly, periodic drug plasma concentration monitoring, effect on ketone and thyroid function tests, effect of HIV and CMV replication, medication in the stool, Stevens-Johnson syndrome (~1:5000). **Metabolism/Pharmacogenomics:** Major metabolic pathways involve glucuronidation and beta-oxidation. **Significant drug-drug interactions:** Check all drug-drug interactions as they are common with this medication and **CONSIDER CONSULTATION WITH A PHARMACIST BEFORE PRESCRIBING THIS MEDICATION.** OF NOTE: aspirin at antipyretic dosages can increase free valproic acid level up to 4X and both carbapenem antibiotics and carbamazepine can significantly increase the clearance of valproic acid. Also, hyperammonemia and encephalopathy are associated with concomitant topiramate use. **Pregnancy: Category X (migraine prophylaxis/D (other indication); associated w/ increased risk of teratogenesis/fetal risk, particularly neural tube defects, other major malformations, and decreased IQ (need to inform women of childbearing age of this risk and recommend birth control) and should be avoided in pregnancy.** **Breastfeeding:** Excreted in breast milk/Use caution. Recommend checking valproic acid blood levels in the infant/toddler to confirm minimal maternal transfer of this medication given the variability in excretion between mothers as well monitoring for excessive bleeding or bruising in the infant/toddler. Also consider periodically checking (e.g., q 6 months) the

infant/toddler's platelets, LFTs, and coagulation tests. **Dosage Form:** Capsule, Coated Tablet (Do not cut, crush or chew), Solution. **Generic Available:** Yes (ER, DR). **Cost:** Divalproex IR: \$; Divalproex ER \$\$ **FDA label information from Drugs @FDA for Depakote ER dated 7.31.2013.**

LAMOTRIGINE (LAMICTAL)

DOSING INFORMATION: Week 1 and 2: **Start:** 25 mg qday. Week 3 and 4: 50 mg qday, if tolerated. Week 5: 100 mg qday, if tolerated. Week 6: 200 mg qday, if tolerated (the **Initial Target and Typical Dose** as there is no compelling evidence of increased mood stabilization benefit at higher doses). Dosage will need to be adjusted for patients taking carbamazepine, phenytoin, phenobarbital, primidone, or valproate (see FDA guidelines). **OF NOTE:** Estrogen containing oral contraceptives increase metabolism of Lamictal such that target dose may need to be increased. Starter packs are available. **Restarting therapy after discontinuation:** If lamotrigine has been withheld for 3 days, restart according to initial dosing recommendations. **Non-urgent discontinuation:** Decrease by 50% per week (over at least 2 weeks).

ONGOING MONITORING: Drug levels are not typically measured.

GENERAL INFORMATION: Mechanism of action: Antiepileptic drug with mood stabilizer efficacy. **FDA Indications:** Bipolar Disorder, maintenance. **Off-Label Indications:** Bipolar, depression. **Pharmacokinetics:** $T_{1/2}$ = 25 hrs.

Common side effects: Nausea (14%), insomnia (10%), fatigue (8%), rhinitis (7%), abdominal pain (6%), constipation (5%), vomiting (5%). **Black Box Warning:** For serious, life-threatening rashes requiring hospitalization and discontinuation of treatment (Stevens-Johnson syndrome @ approx. 1: 1000). Nearly all cases of life-threatening rashes associated with lamotrigine have occurred within 2 to 8 weeks of treatment initiation. The risk of rash may also be increased by co-administration of lamotrigine with Depakote (valproic acid) exceeding the recommended initial dose of lamotrigine, or exceeding the recommended dose escalation for lamotrigine. Lamotrigine should ordinarily be discontinued at the first sign of rash, unless the rash is clearly not drug related.

Contraindications: Known hypersensitivity reaction to the product. **Warnings and Precautions:** Serious skin rashes, multiorgan hypersensitivity reactions and organ failure, blood dyscrasias, suicidal behavior and ideation, increased aseptic meningitis risk, dosage adjustments needed for oral contraceptives, withdrawal seizures, increased risk of status epilepticus, sudden unexplained death in epilepsy. **Metabolism/Pharmacogenomics:** Metabolized primarily by glucuronidation. **Significant drug-drug interactions:** Notable interactions decreasing lamotrigine levels include estrogen containing oral contraceptives (~50%), and carbamazepine (~40%). Valproate increases lamotrigine concentrations slightly more than two-fold. Check all drug-drug interactions before prescribing. **Pregnancy:** Category C; North American Antiepileptic Drug Pregnancy Registry (NAAED) suggest an increased incidence of cleft lip and/or cleft palate following first trimester exposure. **Breastfeeding:** Excreted in breast milk/Not Recommended. **Dosage Form:** Tablet, Chewable, Oral Dissolving Tablet. **Generic Available:** Yes. **Cost:** €. **FDA label information from Drugs @FDA for Lamictal dated 12.20.2013.**

LITHIUM (LITHIUM CARBONATE, IR), LITHIUM-CONTROLLED RELEASE (LITHIUM ER, LITHOBID)

DOSING INFORMATION: Week 1: Check baseline labs (urine pregnancy, basic metabolic panel (baseline Cr), Ca^{2+} , CBC (for baseline WBC) TSH, EKG (for patients over 40 y/o). **Start (IR/ER):** Lithium 300 mg bid or 600 mg qHS (may start with 300 mg/qHS, if the patient is less acute or sensitive to side effects, to increase tolerability). Week 2 and Beyond: Check lithium level weekly (ideally 12 hours after the last dose) and as indicated and tolerated increase dose in 300 mg/day increments to target plasma level of 0.8-1.0 meq/L. **Typical Target Plasma Level and Dose:** Plasma level 0.8-1.0 meq/L which usually equates with daily dose of 1200-1800 mg. **OF NOTE:** For less severe conditions and for maintenance, a target plasma level between 0.6 and 0.8 may be desirable. **Dosing Schedule** should be determined by tolerability and compliance; Typically bid or qHS. **Formulation:** There are both immediate release and sustained release formulations. Nausea is more common with IR formulations and diarrhea with ER formulations. **Discontinuation:** Taper slowly (e.g., 25% per week) to minimize withdrawal symptoms and/or relapse.

ONGOING MONITORING: Check lithium levels 5-7 days after dose change (ideally 12 hours after last dose) and Q6 months when stable. Other labs: Baseline labs as above, Repeat at Q3 months X2 and Q6 months **GENERAL INFORMATION: Mechanism of action:** Natural salt with mood stabilizer efficacy. **FDA Indications:** Bipolar disorder, mania; bipolar disorder, maintenance. **Off-Label Indications:** Bipolar disorder, depression; depression

augmentation; anti-suicide effect. **Pharmacokinetics:** $T_{1/2} = \sim 24$ hrs. **Common Side Effects:** Nausea, tremor, polyuria (related to nephrogenic diabetes insipidus) and thirst, weight gain, loose stools, cognitive impairment (sedation, including changes in memory, concentration, apathy, and decreased creativity). **Black Box Warning:** Toxicity can occur at levels close to therapeutic dosing: Mild symptoms occur at 1.5-2.5 meq/L (increase tremor, slurred speech, and increased lethargy), Moderate 2.5-3.5 meq/L (clonus, coarse tremors, worsening lethargy), and Severe above 3.5 meq/L which can be lethal. **Contraindications:** Known hypersensitivity reaction to the product. Significant renal impairment, significant cardiovascular disease, psoriasis, sodium depletion, dehydration, or debilitation. **Warnings and Precautions:** Lithium toxicity, unmasking of Brugada syndrome (disorder characterized by abnormal EKG findings and a risk of sudden death), renal effects (including long-term diminution of concentrating ability, morphologic changes), encephalopathic syndrome when coadministered with an antipsychotic, concomitant use with neuromuscular blocking agents, increased risk of hypothyroidism and hyperparathyroidism with long term use, drug-drug interactions (see below). **Metabolism/Pharmacogenetics:** Excreted renally. **Significant drug-drug interactions:** Use with a great deal of caution with drugs that increase lithium levels including thiazide diuretics, NSAIDs (except aspirin), ACE-inhibitors, tetracyclines, metronidazole, potassium-sparing diuretics, and loop diuretics. Avoid or use alternatives with most calcium channel blockers. Increased risk of EPS and neurotoxicity with 1st generation antipsychotics. Check all drug-drug interactions before prescribing. **Pregnancy: Category D; associated w/ increased risk of teratogenesis (need to inform women of childbearing age of this risk).** Cardiac malformations, including Epstein's anomaly (background rate of this defect is 1/20,000 births compared to the 1/1000 rate among infants exposed to lithium in utero), are the primary risk of using lithium during the first trimester. **Breastfeeding:** Contraindicated. **Dosage Form:** Capsule, Tablet, Coated Tablet (Do not cut, crush or chew). **Generic Available:** IR/ER: Yes. **Cost:** \$. **FDA label information from Drugs @FDA for Lithobid and lithium carbonate dated 10.20.2011.**

ANTIPSYCHOTICS

ARIPIPRAZOLE (ABILIFY)

ANTIPSYCHOTIC RISK PROFILE: EPS: Mild; TD Risk: Mild; Sedation: Mild; Metabolic Effects: Mild.

DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC), EKG (to assess QTc) and AIMS test. **Initiation for Schizophrenia: Start:** 7.5 mg qday. Week 2: increase dose to an **Initial Target Dose** of 15 mg qday, if tolerated. **Typical Dosage Range:** 15-30 mg qday. **Max Dose:** 30 mg qday, although there is little compelling evidence for benefit of doses above 15 mg qday. **Initiation for Bipolar Manic/Mixed Episode: Start:** 7.5-15 mg qday depending on episode severity. Week 2: Increase dose to an **Initial Target Dosage** between 15-30 mg qday depending on tolerability and response to Abilify. **Typical Dosage Range:** 15-30 mg qday. **Max Dose:** 30 mg qday. **Initiation for Major Depressive Disorder, Adjunctive: Start:** 2 mg qday (the **Initial Target Dose**). Continue for at least 2 weeks. Week 3: Consider further increase to 5 mg qday, if tolerated, and if still severely symptomatic. **Typical Dosage Range:** 2-5 mg qday. **Max Dose:** 10 mg qday. **Discontinuation:** Taper slowly to minimize withdrawal symptoms. **ONGOING MONITORING:** EKG at target dose (at least once to assess QTc). At 4 weeks: weight. At 8 weeks: weight. At 12 weeks: weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: weight. Annually ongoing: waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, and AIMS test. Repeat CBC in patients with previous low WBC.

GENERAL INFORMATION: Atypical antipsychotic/partial dopamine agonist. **FDA Indications:** Schizophrenia; Bipolar mania and mixed episode (also as adjunctive to lithium and valproate); Major depressive disorder, adjunctive; Irritability associated with autism (pediatrics). **Off-Label Indications:** PTSD/OCD augmentation. **Pharmacokinetics:** $T_{1/2} = 75$ h. **Common side effects (MDD, adjunctive):** Akathisia (25%), restlessness (12%), insomnia (8%), fatigue (8%), blurred vision (6%), constipation (5%). **Common side effects (Mania):** Akathisia (13%), sedation (8%), restlessness (6%), tremor (6%), extra-pyramidal symptoms (5%). **Black Box Warnings:** (1) Increased mortality in elderly patients with dementia related psychosis. (2) Increased risk of suicidal thinking and behavior in children, adolescents and young adults. **Contraindications:** Known hypersensitivity reaction to the product. **Warnings and Precautions:** Use in elderly patients with dementia-related psychosis, clinical worsening of depression and suicide risk, NMS, TD, metabolic changes including hyperglycemia and diabetes mellitus,

dyslipidemia and weight gain, orthostatic hypotension, increased risk of leukopenia, neutropenia and agranulocytosis, seizures/convulsions, potential for cognitive and motor impairment, body temperature dysregulation, dysphagia, QTc prolongation, sudden cardiac death, cerebrovascular accident.

Metabolism/Pharmacogenomics: Metabolized by 3A4 and 2D6. **Significant drug-drug interactions:** Caution with 3A4 inducers (e.g., carbamazepine)—Abilify dosage should be doubled when coadministered with carbamazepine. Caution when co-administered with strong 3A4 inhibitors (e.g., ketoconazole and protease inhibitors) and strong 2D6 inhibitors (e.g., fluoxetine and paroxetine). In both cases the Abilify dosage should be cut in half. Potential to enhance the effect of certain antihypertensives due to its α 1-adrenergic receptor antagonism; Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. Developmental toxicity and teratogenic effects in animal studies. **Breastfeeding:** Excreted in breast milk/Not Recommended. **Dosage Form:** Tablet, Soluble, Oral Dissolving Tablet. **Generic Available:** No, **Cost:** \$\$\$ **FDA label information from Drugs @FDA for Abilify dated 7.20.13.**

ASENAPINE (SAPHRIS)

ANTIPSYCHOTIC RISK PROFILE: EPS: Mild to moderate; TD Risk: Unknown; Sedation: Mild to moderate Metabolic Effects: Mild

DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, EKG (to assess QTc) and AIMS test. **Initiation for Schizophrenia: Start:** 5 mg bid (the **Initial Target and Typical Dose**). OF NOTE: This is a sublingual medication and the patient should not eat or drink for 10 min after administration. **Max Dose:** 10 mg bid, although there is little compelling evidence in schizophrenia for additional efficacy of 10 mg bid. **Initiation for Bipolar Manic/Mixed Episode: Start:** 5-10 mg bid (the **Initial Target and Typical Dose**) depending on episode severity. **Typical Dosage Range:** 5-10 mg bid. **Max Dose:** 10 mg bid. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, AIMS test. Repeat CBC in patients with previous low WBC.

GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Acute schizophrenia; Acute bipolar mania or mixed (monotherapy or as adjunctive). **Off-Label Indications:** None. **Pharmacokinetics:** $T_{1/2}$ = 24 hrs. **Common side effects (Schizophrenia):** Somnolence (13%), EPS excluding akathisia (10%), akathisia (6%), oral hypoesthesia (5%).

Black Box Warnings: Increased mortality in elderly patients with dementia related psychosis. **Contraindications:** Known hypersensitivity reaction to the product. **Warnings and Precautions:** Increased mortality and risk of cerebrovascular adverse events including stroke in elderly patients with dementia-related psychosis, NMS, TD, hyperglycemia and diabetes mellitus, weight gain, hypersensitivity reactions, orthostatic hypotension and syncope, increased risk of leukopenia, neutropenia and agranulocytosis, QT prolongation, sudden cardiac death, hyperprolactinemia, seizures, potential for cognitive and motor impairment, body temperature regulation, dysphagia. **Metabolism/Pharmacogenomics:** Cleared primarily by glucuronidation and metabolism by 1A2. **Significant drug-drug interactions:** Saphris is a weak 2D6 inhibitor. Use caution when coadministered with drugs metabolized by 2D6 (e.g., venlafaxine). Caution when coadministered with potent 1A2 inhibitors (e.g., fluvoxamine); Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** No data/Not recommended. **Dosage Form:** Sublingual tablet. **Generic Available:** No. **Cost:** \$\$\$ **FDA label information from Drugs @FDA for Saphris dated 3.21.13.**

HALOPERIDOL (HALDOL)

ANTIPSYCHOTIC RISK PROFILE: EPS: High; TD Risk: High; Sedation: Mild; Metabolic Effects: Mild.

DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, EKG (to assess QTc) and AIMS test. **Start:** haloperidol 1 mg bid (0.5 mg bid in the elderly)*. Week 2: Increase haloperidol to an **Initial Target Dose** of 2 mg bid (1 mg bid in the elderly), if tolerated. Week 3 and beyond: Assess for side effects and consider further increases to 1 mg bid increments, if tolerated, until symptom remission or max dose is reached. If qAM dosage is excessively sedating consider consolidating more of the dose to qHS. **Typical Dosage Range:** 4-10 mg (2-5 mg in the elderly). **Max Dose:** 20 mg (10 mg in the elderly). *OF NOTE: It is frequently necessary to prescribe an anticholinergic medication with Haldol to treat

Parkinsonian side effects (Benadryl 25 mg or Cogentin 1-2 mg PRN or scheduled). **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: weight. At 8 weeks: weight. At 12 weeks: weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: weight. Annually ongoing: waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, and AIMS test.

GENERAL INFORMATION: Typical antipsychotic. **FDA Indications:** "Management of manifestation of psychotic disorders." **Pharmacokinetics:** T_{1/2} = up to 3 weeks. **Common side effects (Psychosis):** Extra-pyramidal symptoms (Parkinsonism, akathisia), orthostatic hypotension, sedation/fatigue, weight gain, dry mouth, nausea, insomnia, dizziness, anxiety. **Black Box Warning:** Increased mortality in elderly patients with dementia related psychosis.

Contraindications: Known hypersensitivity reaction to the product. Severe toxic central nervous system depression or comatose states. Parkinson's disease. **Warnings/Precautions:** Increased risks in elderly patients with dementia-related psychosis, cardiovascular effects (sudden death, QT-prolongation, and torsades de pointes), TD, NMS, usage in pregnancy, combined use with lithium, increased risk of bronchopneumonia, potential for cognitive and motor impairment, use with alcohol, increased risk of leukopenia, neutropenia and agranulocytosis, hypotension, caution in patient with severe cardiovascular disease, seizures, hyperprolactinemia, potential for severe neurotoxicity in patients with thyrotoxicosis, dysphagia, body temperature regulation.

Metabolism/Pharmacogenomics: Metabolized by glucuronidation and 3A4 and 2D6. **Significant drug-drug interactions:** Caution with 3A4 inducers (e.g., carbamazepine and St. John's wort) and inhibitors of 3A4 (ketoconazole and protease inhibitors) and 2D6 (e.g., fluoxetine and paroxetine); Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk/Use caution. Would recommend checking blood levels in the infant/toddler to confirm minimal maternal transfer of this medication given the variability in excretion between mothers. **Dosage Form:** Tablet, Concentrate. **Generic Available:** Yes. **Cost:** [C](#). **FDA label for Haldol from dailymed.nlm.nih.gov, Rev. dated 10.2011.**

ILIOPERIDONE (FANAPT)

ANTIPSYCHOTIC RISK PROFILE: EPS: Very low; TD Risk: Mild; Sedation: Unknown, likely low; Metabolic Effects: Moderate

DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, EKG (to assess QTc) and AIMS test. **Titration schedule:** Day 1: 1 mg bid. Day 3: 2 mg bid. Day 8: 4 mg bid. Day 15: 6 mg bid (the **Initial Target Dose**). Titration can be slowed for orthostatic hypotension or other side effects. Week 3: Consider further titration to max dosing as needed and tolerated.

Typical Dosage Range: 6-12 mg bid. **Max Dose:** 24 mg/day. **Restarting therapy after discontinuation:** if medication has been stopped for greater than 3 days, the initial titration schedule should be followed.

Discontinuation: Taper slowly to minimize withdrawal symptoms.

ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, AIMS test. Repeat CBC in patients with previous low WBC.

GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Schizophrenia. **Off-Label Indications:** None. **Pharmacokinetics:** T_{1/2} = 18 hrs, active metabolite = 26 hrs. **Common side effects:** Dizziness (10%), somnolence (9%), dry mouth 8%), nasal congestion (5%). **Black Box Warnings:** Increased mortality in elderly patients with dementia related psychosis. **Contraindications:** Known hypersensitivity reaction to the product. **Warnings and Precautions:** Increased risks in elderly patients with dementia-related psychosis, QTc prolongation, NMS, TD, metabolic changes including hyperglycemia and diabetes, dyslipidemia and weight gain, seizures, orthostatic hypotension and syncope, increased risk of leukopenia, neutropenia and agranulocytosis, hyperprolactinemia, body temperature regulation, dysphasia, **priapism**, potential for cognitive and motor impairment, sudden cardiac death, cardiovascular accident. **Metabolism/Pharmacogenomics:** Metabolized by 3A4 and 2D6. Caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Caution when co-administered with strong 3A4 inhibitors (e.g., ketoconazole) and strong 2D6 inhibitors (e.g., fluoxetine and paroxetine). In both cases the Fanapt dosage should be cut in half. Caution with centrally acting antihypertensives (due to its α₁-adrenergic receptor

antagonism). Should not be used with any other drugs that prolong the QT interval; Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** No data/Not recommended. **Dosage Form:** Tablet. **Generic Available:** No. **Cost:** \$\$\$\$. **FDA label information from Drugs @FDA for Fanapt dated 4.21.2014.**

LURASIDONE (LATUDA)

ANTIPSYCHOTIC RISK PROFILE: EPS: Mild to Moderate; TD Risk: Unknown; Sedation: Moderate; Metabolic Effects: Mild.

DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC), EKG (to assess QTc) and AIMS test. OF NOTE: It is critical to take Latuda with food (at least 350 calories) for optimal absorption (increased by up to three fold). Also, grapefruit juice should be avoided. **Initiation for Schizophrenia: Start:** 40 mg qday (the **Initial Target Dosage**). Week 2: Assess for side effects. **Typical Dosage Range:** 40-160 mg qday. **Max Dose:** 160 mg/day. **Initiation for Bipolar Depression: Start:** 20 mg qday (the **Initial Target Dose**). Week 2: Assess for side effects. **Typical Dosage Range:** 20-60 mg/day. **Max Dose:** 120 mg/day. **Discontinuation:** Taper slowly to minimize withdrawal symptoms. **ONGOING MONITORING:** EKG at target dose (at least once to assess QTc). At 4 weeks: Weight. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, AIMS test. Repeat CBC in patients with previous low WBC.

GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Schizophrenia; Bipolar I, depression as monotherapy or adjunct to lithium or valproate. **Off-Label Indications:** No data yet. **Pharmacokinetics:** T_{1/2} = 18 hrs. **Common Side Effects (Schizophrenia):** Somnolence (17%), EPS (14%), akathisia (13%), nausea (10%). **Common Side Effects (Bipolar Depression):** Nausea (14%), somnolence (11%), akathisia (9%), EPS (7%). **Black Box Warnings:** (1) Increased mortality in elderly patients with dementia related psychosis. (2) Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants. (3) Monitor for worsening and emergence of suicidal thoughts and behaviors. **Contraindications:** Known hypersensitivity reaction to the product. Coadministration with strong CYP3A4 inhibitors (e.g., ketoconazole and protease inhibitors) and inducers (e.g., carbamazepine and St. John's wort). **Warnings and Precautions:** Increased mortality and risk of cerebrovascular adverse events including stroke in elderly patients with dementia-related psychosis, suicidal thoughts and behaviors in adolescents and young adults, NMS, TD, metabolic changes including hyperglycemia and diabetes, hyperprolactinemia, increased risk of leukopenia, neutropenia and agranulocytosis, orthostatic hypotension and syncope, seizures, potential for cognitive and motor impairment, body temperature dysregulation, hypomanic/manic switch, dysphagia, neurological adverse reactions in patient with Parkinson's disease or dementia with Lewy Bodies. **Metabolism/Pharmacogenomics:** Metabolized by 3A4. **Significant drug-drug interactions:** **Do not use Latuda in combination with strong 3A4 inhibitors (e.g., ketoconazole or protease inhibitors) or inducers (e.g., carbamazepine or St. John's wort).** Latuda dosage should be cut in half with moderate 3A4 inhibitors (e.g., diltiazem). Dosage adjustment may be necessary with coadministered with moderate 3A4 inducers. Grapefruit juice should be avoided. Check all drug-drug interactions and **CONSIDER CONSULTATION WITH A PHARMACIST BEFORE PRESCRIBING THIS MEDICATION.** **Pregnancy:** Category B. **Breastfeeding:** No data/Not recommended. **Dosage Form:** Tablet. **Generic Available:** No. **Cost:** \$\$\$\$. **FDA label information from Drugs @FDA for Latuda dated 7.12.2013.**

OLANZAPINE (ZYPREXA)

ANTIPSYCHOTIC RISK PROFILE: EPS: Mild; TD Risk: Mild; Sedation: Moderate to high; Metabolic Effects: Severe.

DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC), EKG (to assess QTc) and AIMS test. **Initiation for Schizophrenia: Start:** 5 mg qHS. Week 2: Increase dose to the **Initial Target Dose** of 10 mg qHS, if tolerated. Week 3 and beyond: If still symptomatic, consider further increases, if tolerated, to 15-20 mg qHS. **Typical Dosage Range:** 10-20 mg qHS. **Max Dose:** 20 mg qHS. **Initiation for Bipolar Manic/Mixed Episode: Start:** 10 mg qHS (the **Initial Target Dose**). Week 2 and beyond: Increase dose to 15 mg qHS as needed and tolerated. **Typical Dosage Range:** 10-20 mg qHS mg. OF NOTE: Maintenance dosage is usually lower than dose used in acute episodes. **Max Dose:** 20 mg qHS. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight, Fasting lipid profile. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, and AIMS test.

GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Schizophrenia, Bipolar I disorder (manic or mixed episodes) with and without lithium or valproate. **Off-Label Indications:** PTSD/OCD augmentation, Depression augmentation. **Pharmacokinetics:** $T_{1/2}$ = 30 hr. **Common Side Effects:** Weight gain/increased appetite (~17% >11 lb. gain at six weeks; ~40% >11 lb. gain at 6 months), somnolence (29%), dizziness (11%), dry mouth (9%), constipation (9%). **Black Box Warnings:** Increased mortality in elderly patients with dementia related psychosis. **Contraindications:** Known hypersensitivity reaction to the product. **Warnings and Precautions:** Elderly patients with dementia-related psychosis, NMS, hyperglycemia, hyperlipidemia, weight gain, TD, orthostatic hypotension, leukopenia, neutropenia, and agranulocytosis, dysphagia, seizures, potential for cognitive and motor impairment, body temperature dysregulation, hyperprolactinemia, QT prolongation, sudden cardiac death, cerebrovascular accident. **Metabolism/Pharmacogenomics:** Primarily metabolized by direct glucuronidation and 1A2. **Significant drug-drug interactions:** Caution when coadministered with 1A2 inducers (e.g., carbamazepine) and potent 1A2 inhibitors (e.g., fluvoxamine—consider dosage adjustment); **OF NOTE:** tobacco induces the metabolism of Zyprexa—consider dosage adjustment when starting or stopping tobacco; Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk /Not recommended. **Dosage Form:** Tablet, Tablet Dispensible. **Generic Available:** Yes. Cost: €. **FDA label information from Drugs @FDA for Zyprexa dated 7.12.2013.**

OLANZAPINE AND FLUOXETINE (SYMBYAX):

ANTIPSYCHOTIC RISK PROFILE: EPS: Mild TD Risk: Mild Sedation: Moderate to high Metabolic Effects: Severe
DOSING INFORMATION: **Initiation for Bipolar Depression and Treatment Resistant Depression:** Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, EKG (to assess QTc) and AIMS test. Consider BMP for baseline sodium in older adults. **Start:** olanzapine 6 mg /fluoxetine 25 mg qHS (the **Initial Target Dose**). In patients with risk for orthostasis, start olanzapine 3 mg/fluoxetine 25 mg qHS. Week 4 and beyond: Consider increase in dose if needed and tolerated. **Typical Dosage Range:** olanzapine 6 mg/fluoxetine 25 mg-olanzapine 12 mg/fluoxetine 50 mg qHS. **Max Dose:** olanzapine 12 mg /fluoxetine 50 mg qHS. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight, Fasting lipid profile. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, AIMS test. Repeat CBC in patients with previous low WBC. Consider posttreatment BMP to rule out hyponatremia in older adults.

GENERAL INFORMATION: Atypical antipsychotic combined with SSRI. **FDA Indications:** Depressive Episodes Associated with Bipolar I disorder and Treatment Resistant Depression. **Off-Label Indications:** None. **Pharmacokinetics:** $T_{1/2}$ (olanzapine) = 30 hr; $T_{1/2}$ (fluoxetine) = 4-6 days. **Common Side Effects:** Somnolence (27%), Weight gain (25%), increased appetite (20%), dry mouth (15%), edema (15%), fatigue (12%), tremor (9%), vision blurred (5%), disturbance in attention (5%). **Black Box Warnings:** (1) Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants, (2) Monitor for worsening and emergence of suicidal thoughts and behaviors, (3) Increased mortality in elderly patients with dementia related psychosis. **Contraindications:** Known hypersensitivity reaction to fluoxetine or olanzapine. Use of a MAOI within 5 weeks of stopping Symbyax, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Symbyax within 5 weeks of stopping a MAOI. Do not use pimozide or thioridazine with Symbyax because of QT prolongation risk. **Warnings and Precautions:** Clinical worsening and suicide risk, elderly patients with dementia-related psychosis, NMS, hyperglycemia, hyperlipidemia, weight gain, serotonin syndrome, allergic reactions and rash, hypomanic/manic switch, TD, orthostatic hypotension, leukopenia, neutropenia, and agranulocytosis, dysphagia, seizures, abnormal bleeding, hyponatremia, potential for cognitive and motor impairment, body temperature dysregulation, QT prolongation, hyperprolactinemia, long elimination half-life of fluoxetine, discontinuation reactions, sudden cardiac death, cerebrovascular accident. **Metabolism/**

Pharmacogenomics: Fluoxetine: primarily metabolized by 2D6. Use caution with 2D6 poor metabolizers. Olanzapine: primarily metabolized by direct glucuronidation and 1A2. **Significant drug-drug interactions:** Fluoxetine: potent 2D6 inhibitor; Use significant caution when coadministered with drugs metabolized by 2D6 (e.g., TCAs). Olanzapine: caution when coadministered with 1A2 inducers (e.g., carbamazepine) and potent 1A2 inhibitors (e.g., fluvoxamine—consider dosage adjustment). OF NOTE: tobacco induces the metabolism of olanzapine—consider dosage adjustment when starting or stopping tobacco. Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk/Not recommended. **Dosage Form:** Capsule. **Significant drug-drug interactions:** Check all drug-drug interactions. **Generic Available:** Yes. **Cost:** \$\$ (if components purchased separately, \$). **FDA label information from Drugs @FDA for Symbyax dated 8.7.2013.**

PALIPERIDONE (INVEGA)—ORAL FORMULATION

ANTIPSYCHOTIC RISK PROFILE: EPS: Moderate; TD Risk: Moderate; Sedation: Moderate; Metabolic Effects: Moderate.

DOSING INFORMATION: **Initiation for Schizophrenia and Schizoaffective Disorder:** Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, and EKG (to assess QTc) and AIMS test. **Start:** 3 mg qAM. Week 2: Increase to an **Initial Target Dose** of 6 mg qAM, if tolerated. Week 3 and beyond: Consider further increases in 3 mg increments up to a maximum of 12 mg/day, if tolerated. **Typical Dosage Range:** 3-12 mg qday. **Max Dose:** 12 mg/day. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, AIMS test. Repeat CBC in patients with previous low WBC.

GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Schizophrenia; Schizoaffective disorder (monotherapy or as adjunctive). **Off-Label Indications:** Bipolar, mixed or manic. **Pharmacokinetics:** T_{1/2} = 23 hrs. **Common Side Effects (Schizophrenia):** Somnolence (20%), extra-pyramidal symptoms (18%), akathisia (11%), tachycardia (9%). **Black Box Warnings:** Increased mortality in elderly patients with dementia related psychosis. **Contraindications:** Known hypersensitivity reaction to the product or to risperidone, or to any components in the formulation. **Warnings and Precautions:** Increased mortality and risk of cerebrovascular adverse events including stroke in elderly patients with dementia-related psychosis, NMS, QT prolongation, sudden cardiac death, cerebrovascular accidents, TD, metabolic changes including hyperglycemia and diabetes, dyslipidemia and weight gain, hyperprolactinemia, potential for gastrointestinal obstruction, orthostatic hypotension and syncope, increased risk of leukopenia, neutropenia and agranulocytosis, potential for cognitive and motor impairment, seizures, dysphagia, **priapism**, potential increased risk for thrombotic thrombocytopenic purpura, body temperature dysregulation, antiemetic effect. **Metabolism/Pharmacogenomics:** Majority of absorbed dose is renally excreted unchanged. Multiple minor hepatic metabolic pathways. **Significant drug-drug interactions:** Caution with use of other drug that can cause orthostatic hypotension; Carbamazepine increases the renal clearance of Invega by ~40% whereas valproate increases the effective dosage of Invega by ~50%. Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk /Not recommended. **Dosage Form:** Tablet, Suspension. **Generic Available:** No. **Cost:** \$\$\$ **FDA label information from Drugs @FDA for INVEGA dated 4.6.2011.**

PERPHENAZINE (TRILAFON)

ANTIPSYCHOTIC RISK PROFILE: EPS: Moderate; TD Risk: High; Sedation: Moderate; Metabolic Effects: Mild.

DOSING INFORMATION: Week 1: Assess baseline Weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC) and EKG (to assess QTc) and AIMS test. **Start:** 4 mg bid. Week 2: Increase to an **Initial Target Dose** of 8 mg bid, if tolerated. Week 3 and beyond: Assess for side effects and consider further increases to 12 mg bid if still symptomatic. If qAM dosage is excessively sedating consider consolidating more of the dose to qHS. **Typical Dosage Range:** 8-24 mg/day. **Max Dose:** 24 mg/day in an outpatient setting. OF NOTE: Consider lower overall dosing in the elderly. **Discontinuation:** Taper slowly to

minimize withdrawal symptoms

ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile and AIMS test.

GENERAL INFORMATION: Typical antipsychotic. **FDA Indications:** Schizophrenia. **Pharmacokinetics:** T_{1/2} = 9-12 hrs.

Common Side Effects: Extra-pyramidal symptoms (seen at higher doses; Parkinsonism, akathisia), orthostatic hypotension, sedation/fatigue and anticholinergic side effects (blurred vision, urinary retention, xerostomia, constipation). **Black Box Warnings:** Increased mortality in elderly patients with dementia related psychosis.

Contraindications: Known hypersensitivity reaction to the product. Use in comatose or greatly obtunded patients and in patients receiving large doses of CNS depressants, in patients with suspected or established subcortical brain damage, with or without hypothalamic damage, in the presence of existing blood dyscrasias, bone marrow depression, or liver damage. **Warnings/Precautions:** Increased mortality and risk of cerebrovascular adverse events including stroke in elderly patients with dementia-related psychosis, tardive dyskinesia, NMS, suicidality, seizures, caution in patient with depression, potential for cognitive and motor impairment, orthostatic hypotension, QTc prolongation, hyperprolactinemia, sudden cardiac death, cerebrovascular accident, body temperature dysregulation, increased risk of leukopenia, neutropenia and agranulocytosis long term use associated with potential liver damage, corneal and lenticular deposits. **Metabolism/Pharmacogenomics:** Metabolized by 2D6. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Use caution with potent 2D6 inhibitors (e.g., fluoxetine and paroxetine). Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** Excreted in breast milk /Not recommended. **Dosage Form:** Tablet. **Generic Available:** Yes. **Cost:** \$. **FDA label information from Drugs @FDA for Trilafon dated 5.2.2002. FDA label for perphenazine from dailymed.nlm.nih.gov, Rev. dated 12.2013.**

QUETIAPINE (SEROQUEL (IR), SEROQUEL XR)

ANTIPSYCHOTIC RISK PROFILE: EPS: Mild; TD Risk: Mild; Sedation: Moderate; Metabolic Effects: Moderate to severe.

DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC), EKG (to assess QTc) and AIMS test. **Initiation for Schizophrenia or Bipolar Manic/Mixed Episode:** Start Seroquel-IR: Day 1, 25 mg bid; Day 2, 50 mg bid; Day 3, 100 mg bid; Day 4, 150 mg bid and Day 5, 200 mg bid (**Initial Target Dose IR**). This titration schedule can be slowed down because of side effects. At higher daily dosages consider scheduling a greater proportion of dose qHS to limit daytime sedation. **Start Seroquel-XR:** Day 1, 50 mg qHS; Day 2, 100 mg qHS; Day 3, 200 mg qHS; Day 4, 300 mg qHS and Day 5, 400 mg qHS (**Initial Target Dose XR**). This titration schedule can be slowed down because of side effects. Week 2: Can consider further increases in 100 mg increments, if tolerated, up to **Max Dose (IR/XR)** of 800 mg/day. **Typical Dosage Range (IR/XR):** 400-800 mg/day. **Initiation for Bipolar Depression:** Start Seroquel IR/XR: Day 1, 50 mg qHS; Day 2, 100 mg qHS; Day 3, 200 mg qHS; and Day 4, 300 mg qHS (**Initial Target Dose IR/XR**). **Typical Dosage Range (IR/XR):** 300-600 mg/day. **Max Dose (IR/XR):** 600 mg/day. **Initiation for Adjunctive Treatment for Major Depression:** Start Seroquel XR: Day 1, 50 mg qHS; Day 2, 100 mg qHS; Day 3, 150 mg qHS (**Initial Target Dosage XR**). **Typical Dosage Range (XR):** 150-300 mg qHS. **Maximum Dose (XR):** 300 mg qHS. OF NOTE: for the elderly consider a slower rate of dose titration and a lower target dose for all indications.

Discontinuation: Stopping medication abruptly may cause discontinuation syndrome (insomnia, nausea, headache, diarrhea, vomiting, irritability).

ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight, Fasting lipid profile. At 8 weeks: weight. At 12 weeks: weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: weight. Annually /ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile and AIMS test. Consider checking for cataracts.

GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Schizophrenia (IR, XR), Bipolar I – manic (IR, XR), Bipolar I – mixed (XR), Bipolar disorder – depressive episode (IR, XR), Bipolar maintenance as adjunctive to lithium or divalproex (IR, XR), Adjunctive treatment of MDD (XR). **Off-Label Indications:** Anxiety disorders augmentation. **Pharmacokinetics:** T_{1/2} = 6 hr (IR); 7 hrs (XR). **Common Side Effects (Schizophrenia and Bipolar**

Mania—Seroquel IR: Headache (21%), somnolence (18%), dizziness (11%), dry mouth (9%), constipation (8%), weight gain (5%), dyspepsia (5%), ALT increased (5%). **Common Side Effects (Bipolar Depression—Seroquel XR):** Somnolence (52%), dry mouth (37%), Increased appetite (12%), dyspepsia (7%), weight gain (7%), fatigue (6%). **Black Box Warnings:** (1) Increased mortality in elderly patients with dementia related psychosis. (2) Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants. (3) Monitor for worsening and emergence of suicidal thoughts and behaviors. **Contraindications:** Known hypersensitivity reaction to the product. **Warnings and Precautions:** Increased mortality and risk of cerebrovascular adverse events including stroke in elderly patients with dementia-related psychosis, suicidal thoughts and behaviors in adolescents and young adults, NMS, metabolic changes including hyperglycemia and diabetes, dyslipidemia and weight gain, TD, hypotension, increased risk of leukopenia, neutropenia and agranulocytosis, cataracts, QT prolongation, seizures, hypothyroidism, hyperprolactinemia, potential for cognitive and motor impairment, body temperature dysregulation, dysphagia, discontinuation syndrome, seizures, dysphagia QTc prolongation, sudden cardiac death, cerebrovascular accident. **Metabolism/Pharmacogenomics:** Metabolized by 3A4. **Significant drug-drug interactions:** Dosage adjustment is required when quetiapine is coadministered with strong 3A4 inhibitors (e.g., reduce the dosage to one sixth with ketoconazole and ritonavir) or with chronic treatment (>7-14 days) with potent 3A4 inducers (e.g., increase the dosage by 5 fold with phenytoin, rifampin, St. John's wort). Caution with medications that cause QTc prolongation. Check all drug-drug interactions and **CONSIDER CONSULTATION WITH A PHARMACIST BEFORE PRESCRIBING THIS MEDICATION.** **Pregnancy:** Category C. **Breastfeeding:** E Excreted in breast milk /Not recommended. **Dosage Form:** Tablet, Tablet-24-hour. **Generic Available:** IR: yes; XR: No. **Cost:** IR: \$, XR: \$\$\$ **FDA label information from Drugs @FDA for Seroquel IR dated 10.29.14. FDA label information from Drugs @FDA for Seroquel XR dated 4.30.2013.**

RISPERIDONE (RISPERDAL)

ANTIPSYCHOTIC RISK PROFILE: EPS: Moderate; TD Risk: Moderate; Sedation: Moderate; Metabolic Effects: Moderate.

DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC), EKG (to assess QTc) and AIMS test. **Initiation for Schizophrenia: Start:** 1 mg qHS. Week 2: Increase risperidone to 1 mg bid, if tolerated. Week 3: Increase to an **Initial Target Dose** of 1 mg qAM and 2 mg qHS, if tolerated. If qAM dosage is excessively sedating consider consolidating more of the dose to qHS. Week 4 and beyond: Assess side effects and consider further increases in 1 mg increments, if tolerated until symptom remission or **Max Dose** of 6 mg reached. **Typical Dosage Range:** 3-4 mg/day. OF NOTE: dosages above 4 mg/day are much more likely to be associated with EPS and it may be necessary to prescribe an anticholinergic medication to deal with Parkinsonian side effects (Benadryl 25 mg or Cogentin 1-2 mg PRN or scheduled). **Initiation for Bipolar Mania and Mixed Episodes: Start:** 1-2 mg/day (bid or qHS) depending on episode severity. Week 2: Increase to an **Initial Target Dose** of 2-3 mg/day (with more at HS), if tolerated and depending on episode severity. Week 3 and beyond: Assess for side effects and consider further increases in 1 mg increments until symptom remission or **Max Dose** of 6 mg reached. If qAM dosage is excessively sedating consider consolidating more of the dose to qHS. In severe cases of mania consider accelerating this titration schedule. **Typical Dosage Range:** 1-4 mg/day. OF NOTE: dosages above 4 mg/day are much more likely to be associated with EPS and it may be necessary to prescribe an anticholinergic medication to deal with Parkinsonian side effects (Benadryl 25 mg or Cogentin 1-2 mg PRN or scheduled). **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, and AIMS test.

GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Bipolar mania and mixed episode; Schizophrenia. **Off-Label Indications:** Depression augmentation, anxiety disorders augmentation.

Pharmacokinetics: T_{1/2} = 3 hrs for risperidone and 21 hours the active metabolite. **Common side effects (mania):** Parkinsonism (25%), sedation (11%), akathisia (9%), tremor (6%), dystonia (5%), nausea (5%). **Black Box Warnings:** Increased mortality in elderly patients with dementia related psychosis. **Contraindications:** Known

hypersensitivity reaction to the product. **Warnings and Precautions:** Increased mortality and risk of cerebrovascular adverse events including stroke in elderly patients with dementia-related psychosis, NMS, TD, metabolic changes including hyperglycemia and diabetes, dyslipidemia and weight gain, hyperprolactinemia, orthostatic hypotension, increased risk of leukopenia, neutropenia and agranulocytosis, cataracts, potential for cognitive and motor impairment, seizures, dysphagia, **priapism**, body temperature dysregulation, patients with phenylketonuria, QTc prolongation, sudden cardiac death, cerebrovascular accident.

Metabolism/Pharmacogenomics: Metabolized by 2D6 and 3A4 (minor). Use caution with 2D6 poor metabolizers.

Significant drug-drug interactions: The dosage of Risperdal should be adjusted with 2D6 inhibitors (e.g., fluoxetine, and paroxetine) and enzyme 3A4 inducers (e.g., carbamazepine and St. John's wort). See the FDA label for specific recommendations. Check all drug-drug interactions before prescribing. **Pregnancy:** Category C.

Breastfeeding: Excreted in breast milk /Not recommended. **Dosage Form:** Solution, Tablet, Dispersible Tablet.

Generic available: Yes. **Cost:** **¢.** **FDA label information from Drugs @FDA for Risperdal 4.18.2014.**

ZIPRASIDONE (GEODON)

ANTIPSYCHOTIC RISK PROFILE: EPS: Moderate; TD Risk: Mild; Sedation: Moderate; Metabolic Effects: Mild.

DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC), CMP for patients at risk of significant electrolyte disturbances should have baseline serum potassium and magnesium measurements and EKG (to assess QTc) and AIMS test. **Initiation for Schizophrenia: Start:** 20 mg twice daily (with food). Week 2 and beyond: Consider increasing dose by 20 mg bid per week as needed and tolerated. **Typical Dosage Range:** 20-80 mg bid. **Initiation for Bipolar Mania and Mixed Episodes: Start:** 40 mg bid (with food). Week 2 and beyond: Increase dose in 20 mg bid per week increments as needed and tolerated. In severe cases of mania consider accelerating this titration schedule (can increase to 60-80 mg bid on day 2 of treatment if needed). **Typical Dosage Range:** 40-80 mg bid (Mean ~60 mg bid). **Max Dose:** 100 mg bid. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

ONGOING MONITORING: EKG at target dose (at least once to assess QTc). Ziprasidone should be discontinued in patients who are found to have persistent QTc measurements >500 msec. At 4 weeks: Weight. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, and AIMS test.

GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Treatment of schizophrenia. Acute treatment of a mixed or manic episode in bipolar I disorder. Bipolar I disorder maintenance therapy as an adjunct to lithium or valproate. **Off-Label Indications:** Schizoaffective disorder. **Pharmacokinetics:** T_{1/2} = 7 hrs. **Common Side Effects (Schizophrenia):** Somnolence (14%), extrapyramidal symptoms (14%), nausea (10%), respiratory track infection (8%), dizziness (8%). **Black Box Warnings:** Increased mortality in elderly patients with dementia related psychosis.

Contraindications: Known hypersensitivity reaction to the product. Do not use in patients with (1) a known history of QT prolongation, (2) a recent acute myocardial infarction, (3) with uncompensated heart failure. Do not use in combination with other drugs that have demonstrated QT prolongation. **Warnings and Precautions:** Increased mortality in elderly patient with dementia-related psychosis, QT prolongation and risk of sudden death, NMS, TD, metabolic changes including hyperglycemia and diabetes, rash, orthostatic hypotension, increased risk of leukopenia, neutropenia and agranulocytosis, seizures, dysphagia, hyperprolactinemia, potential for cognitive and motor impairment, **priapism**, body temperature dysregulation, cerebrovascular accident.

Metabolism/Pharmacogenomics: Primarily metabolized by aldehyde oxidase. Some metabolism via 3A4.

Significant drug-drug interactions: **Methadone, and any medications that prolong the QT interval are contraindicated.** Potent 3A4 inhibitors (e.g., ketoconazole) and inducers (e.g., carbamazepine) increase and decrease Geodon levels by approximately 35-40% respectively. Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Breastfeeding:** No data/Not recommended. **Dosage Form:** Capsule. **Generic available:** Yes. **Cost:** **\$\$.** **FDA label information from Drugs @FDA for Geodon 12.17.2013.**

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